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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: U.S. Patent No. RE38,551 (Reissue of U.S. Patent No. 5,773,475)
Inventor: KOHN, Harold
Original Issue Date: June 30, 1998
Reissue Issue Date: July 6, 2004
For: ANTICONVULSANT ENANTIOMERIC AMINO ACID
DERIVATIVES
Assignee: Research Corporation Technologies, Inc.
Date: December 23, 2008
Attorney Docket: 32555-0002-1
NDA: NDA 22-253 (VIMPAT[®] tablet)

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL FOR APPLICATION FOR EXTENSION OF PATENT

Sir:

Transmitted herewith for filing is an Application For Extension of Patent Term Under 35 U.S.C. §156 with respect to the above-identified patent.

Applicant, the assignee of the above-referenced patent, on this day has filed simultaneously four related applications for extension of patent term under 35 U.S.C. §156, including the present application referenced in the header above. These four patent term extension applications relate to different combinations of U.S. Patent nos. Re38,551 and 5,654,301 and FDA approvals for New Drug Application nos. NDA 22-253 and NDA 22-254. The four patent term extension applications are summarized in the following table.

12/24/2008 NNGUYEN1 00000026 501349 RE38551
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Attorney Docket No.	Patent No.	NDA No.	Approved Product
32555-0002-1	Re38,551	NDA22-253	VIMPAT [®] (lacosamide) tablet
32555-0002-2	5,654,301	NDA 22-254	VIMPAT [®] (lacosamide) injection
32555-0002-3	Re38,551	NDA 22-254	VIMPAT [®] (lacosamide) injection
32555-0002-4	5,654,301	NDA 22-253	VIMPAT [®] (lacosamide) tablet

Applicant asserts that it has the right, under 35 U.S.C. § 156, to extend two patents relating to VIMPAT[®] (lacosamide) because two NDAs, NDA 22-253 and NDA 22-254 for VIMPAT[®] (lacosamide) tablet and VIMPAT[®] (lacosamide) injection, respectively, were approved on the same day, namely October 28, 2008, and because there were no approvals of lacosamide that occurred prior to October 28, 2006. As such, Applicant has submitted the above four applications for patent term extension with the goal of ultimately obtaining one patent term extension for each of U.S. Patent nos. Re38,551 and 5,654,301.

Applicant respectfully requests that if the Commissioner determines that both of U.S. Patent nos. Re38,551 and 5,654,301 are entitled to a patent term extension under the same regulatory review period or periods (i.e., for the same NDA(s)), and/or determines that at least one of U.S. Patent nos. Re38,551 and 5,654,301 is entitled to a patent term extension under both regulatory review periods (i.e., for both of the two NDA approvals), that the Commissioner establish a time period in accord with the policies set forth in MPEP § 2761 within which the Applicant will be permitted to elect the patent and product combination(s) for which extension is desired and/or to voluntarily withdraw applications. At that time, Applicant will elect and withdraw applications for patent term extension, as appropriate, to ensure that only one patent is extended for each NDA, and such that a given patent obtains only one extension under 35 U.S.C. § 156.

Applicant respectfully requests that if the Commissioner does not share Applicant's view that it is entitled under 35 U.S.C. § 156 to extend a different patent for each of the two above-identified simultaneously-approved NDAs, that the Commissioner direct the Office to contact the undersigned attorney.

In light of the above, and in accordance with the requirements of 35 U.S.C. § 156, attached for the patent and NDA approval identified in the above header are the following:

- 1) Application For Extension of Patent Term (including Exhibits A-F) – application 13 pages and Exhibits 192 pages for 205 pages total;
- 2) Extra copy 1 of Application for Extension of Patent Term (including Exhibits A-F) – application 13 pages and Exhibits 192 pages for 205 pages total; and
- 3) Extra copy 2 of Application for Extension of Patent Term (including Exhibits A-F) – application 13 pages and Exhibits 192 pages for 205 pages total.

☒ Please charge my Deposit Account No. 50-1349 the amount of \$1,120.00, which is believed to be the appropriate fee for a patent term extension as established by 37 C.F.R. § 1.20(j),.

☒ The Commissioner is hereby authorized to charge payment of any fees associated with or necessary for the prosecution of this patent term extension application, including debiting any deficit or crediting any overpayment relating to the fee identified above, to Deposit Account No. 50-1349.

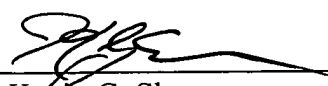
Respectfully submitted,

HOGAN & HARTSON LLP

Dated: December 23, 2008

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By: _____


Kevin G. Shaw
Registration No. 43,110



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: U.S. Patent No. RE38,551 (Reissue of U.S. Patent No. 5,773,475)
Inventor: KOHN, Harold
Original Issue Date: June 30, 1998
Reissue Issue Date: July 6, 2004
For: ANTICONVULSANT ENANTIOMERIC AMINO ACID
DERIVATIVES
Assignee: Research Corporation Technologies, Inc.
Date: December 23, 2008

Attorney Docket: 32555-0002-1

NDA: NDA 22-253 (VIMPAT[®] tablet)

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPLICATION FOR EXTENSION OF PATENT

TERM UNDER 35 U.S.C. §156

Commissioner for Patents:

Applicant, Research Corporation Technologies, Inc., a non-profit corporation organized and existing under the laws of Delaware, and having a principal place of business at 5210 E. Williams Circle, Suite 240, Tucson, Arizona 85711-4410, represents that it is the owner of the entire interest in and to U.S. Patent No. Re38,551, granted to Harold Kohn for "Anticonvulsant Enantiomeric Amino Acid Derivatives," as reflected in the assignment document recorded by the U.S. Patent and Trademark Office on May 22, 1997 at Reel 008538, Frame 0093. Attached at **Exhibit A** is a Power of Attorney document appointing the undersigned patent attorney as legal representative of Applicant.

Schwarz Biosciences, Inc. ("Schwarz"), a corporation of the state of Delaware and having a place of business at 1209 Orange St., Wilmington, DE 19801, is the owner of a New Drug Application ("NDA") for VIMPAT[®] tablet, NDA number NDA 22-253. Schwarz Pharma AG ("SPAG"), having its registered office at Alfred-Nobel Strasse 10, 40789 Monheim, Germany, has exclusive license rights under U.S. Patent No. Re38,551 to lacosamide, R-2-Acetamido-N-benzyl-3-methoxypropionamide. Schwarz and SPAG are related companies, being wholly owned by UCB S.A., which has its registered office at Allée de la Recherche 60, 1070 Brussels, Belgium. Attached at **Exhibit B** is a Letter of Reliance document granting the Applicant from Schwarz Biosciences, Inc. the right to rely upon NDA 22-253 and the activities of SPAG and its predecessors in interest¹ supporting FDA approval of VIMPAT[®] tablet for purposes of obtaining any and all patent term extensions available in conjunction with the approval of VIMPAT[®] tablet.

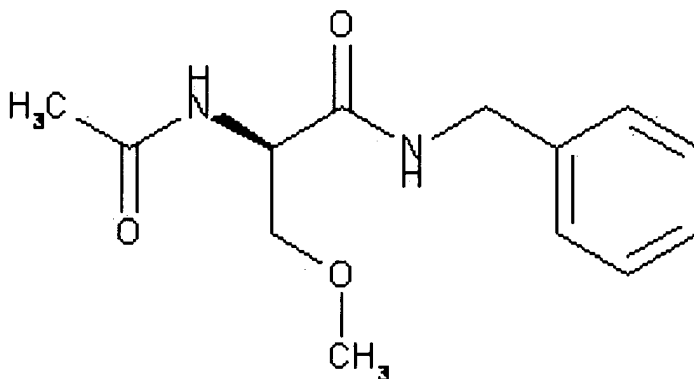
Applicant, acting through its duly authorized attorney, hereby submits this application for extension of patent term under 35 U.S.C. §156, based upon the approval by the Food and Drug Administration for commercial marketing or use of VIMPAT[®] tablet, since the active ingredient of VIMPAT[®] tablet is lacosamide and lacosamide falls within the ambit of the claims of U.S. Patent No. Re38,551. The information contained in this Application and its Exhibits is provided in accordance with the rules promulgated by the U.S. Patent and Trademark Office at 37 CFR §§1.710-1.785 and presented in the manner set forth at 37 CFR §1.740.

1. A Complete Identification Of The Approved Product As By Appropriate Chemical And Generic Name, Physical Structure Or Characteristics

The approved product, VIMPAT[®] tablet, contains lacosamide as its active ingredient and is indicated for adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older. The IUPAC chemical name of lacosamide is (R)-2-acetamido-N-benzyl-3-methoxypropionamide. Lacosamide has the empirical formula

¹ Harris FRC Corp., also a licensee of U.S. Patent No. Re38,551, originally filed the IND (IND 57,939) that ultimately led to NDA 22-253 and subsequent approval of VIMPAT[®] (lacosamide) tablet. That IND and all rights thereto, along with patent license rights, were subsequently transferred to Schwarz and SPAG, respectively, as detailed in Exhibit B and Exhibit F.

$C_{13}H_{18}N_2O_3$, and has a molecular weight of 250.30. Lacosamide is present in VIMPAT[®] in the form of its single (R)-enantiomer, and has the structural formula:



Lacosamide is prepared as a white to light yellow powder that is sparingly soluble in acetonitrile and ethanol. The approved product is formulated as tablets in four different dosages, 50 mg, 100 mg, 150 mg, and 200 mg, for daily oral administration. The initial recommended dosage regimen is one 50 mg tablet twice daily (for 100 mg per day), and dosage can be increased, such as at weekly intervals of 100 mg/day as two equally divided doses, until a maintenance dose of 200 to 400 mg/day (based upon individual patient response and tolerability) is reached. VIMPAT[®] tablets contain the following inactive ingredients: colloidal silicon dioxide, crospovidone, hydroxypropylcellulose, hypromellose, lecithin, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, talc, titanium dioxide, and dye pigments.

2. A Complete Identification Of The Federal Statute Including The Applicable Provisions Of Law Under Which The Regulatory Review Occurred

The approved product, VIMPAT[®] tablet, was subject to regulatory review under Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §355).

3. An Identification Of The Date On Which The Product Received Permission For Commercial Marketing Or Use Under The Provision Of Law Under Which The Applicable Regulatory Review Period Occurred

The approved product, VIMPAT[®] tablet, received permission for commercial marketing or use under Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §355) on October 28, 2008. A copy of a letter from the Food and Drug Administration ("FDA") indicating the date of approval is attached hereto at **Exhibit C**.

4. In The Case Of A Drug Product, An Identification Of Each Active Ingredient In The Product And As To Each Active Ingredient, A Statement That It Has Not Been Previously Approved For Commercial Marketing Or Use Under The Federal Food, Drug, and Cosmetic Act, The Public Health Service Act, Or The Virus-Serum-Toxin Act, Or A Statement Of When The Active Ingredient Was Approved For Commercial Marketing Or Use (Either Alone Or In Combination With Other Active Ingredients), The Use For Which It Was Approved, And The Provision Of Law Under Which It Was Approved

The active ingredient in VIMPAT[®] tablet is lacosamide, which has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

5. A Statement That The Application Is Being Submitted Within The Sixty Day Period Permitted For Submission Pursuant to 37 CFR §1.720(f) And An Identification Of The Date Of The Last Day On Which The Application Could Be Submitted

This application is being submitted within the permitted sixty (60) day period, the last day of which is December 26, 2008.

6. A Complete Identification Of The Patent For Which An Extension Is Being Sought By The Name Of The Inventor, The Patent Number, The Date Of Issue, And The Date Of Expiration

The complete identification of the patent for which extension is sought is:

Inventor:	Harold Kohn
Patent Number:	Re38,551 (a Reissue of U.S. 5,773,475)
Issue Date of U.S. 5,773,475:	June 30, 1998
Expiration Date:	March 17, 2017 (without extension under 35 U.S.C. §156)

7. A Copy Of The Patent For Which An Extension Is Being Sought, Including The Entire Specification (Including Claims) And Drawings

A complete copy of U.S. Patent No. Re38,551 is annexed as **Exhibit D**.

8. A Copy Of Any Disclaimer, Certificate of Correction, Receipt Of Maintenance Fee Payment, Or Reexamination Certificate Issued In The Patent

The patent for which extension is being sought has not been the subject of any disclaimer, certificate of correction, or reexamination certificate. The first maintenance fee was duly paid on September 28, 2001 by Applicant (for U.S. Patent 5,773,475), and the second maintenance fee was duly paid on November 23, 2005 by Applicant, and the next maintenance fee is due to be paid by December 31, 2009. No additional maintenance fees are due at this time. Copies of the maintenance fee statements evidencing this status are annexed as **Exhibit E**.

9. A Statement That The Patent Claims The Approved Product Or A Method Of Using Or Manufacturing The Approved Product, And A Showing Which Lists Each Applicable Patent Claim And Demonstrates The Manner In Which At Least One Such Patent Claim Reads On The Approved Product Or Method Of Using Or Manufacturing The Approved Product

U.S. Patent No. Re38,551 claims the approved product, VIMPAT® tablet. More specifically, claims 1-5 and 7-9 read on the approved product and claim the active ingredient of the final approved product lacosamide, claim 10 reads on the approved product and claims a therapeutic composition comprising lacosamide, and claims 11-13 read on methods that comprise using lacosamide for treatment of central nervous system disorders. Claim 1, covering a compound, is compared to the approved product in the table below.

Patent Claim	Approved Product
<p>1. A compound in the R configuration having the formula:</p> $\text{Ar}-\text{CH}_2\text{NHC}(=\text{O})-\underset{\underset{\text{CH}_2}{ }}{\overset{\text{H}}{\text{C}}}-\underset{\underset{\text{Q}}{ }}{\overset{\text{H}}{\text{N}}}-\text{C}(=\text{O})-\text{Q}_1$	<p>The active ingredient of the approved product is lacosamide, which is (R)-2-acetamido-N-benzyl-3-methoxypropionamide. Lacosamide has an R configuration, and has the structural formula identified above in Section 1 of this application. Comparison of the structural formula above with that in claim 1 shows that the benzene ring at the far right of</p>

wherein Ar is phenyl which is unsubstituted or substituted with at least one halo group; Q is lower alkoxy, and Q ₁ is methyl.	the structure in Section 1 satisfies the unsubstituted phenyl "Ar," the -OCH ₃ group at the bottom of the structure in Section 1 satisfies the lower alkoxy "Q," and the -CH ₃ group at the far left of the structure in Section 1 satisfies the methyl "Q ₁ ."
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Claim 10, covering a therapeutic composition, is compared to the approved product in the table below.

Patent Claim	Approved Product
10. A therapeutic composition comprising an anticonvulsant effective amount of a compound according to any one of claims 1-9 and a pharmaceutical carrier therefor.	The active ingredient of the approved product is lacosamide, and lacosamide falls within the scope of claim 1 as indicated above. The approved product is a tablet that contains a pharmaceutical carrier, such as hydroxypropylcellulose and microcrystalline cellulose.

Claim 11, covering a method of treating central nervous system disorders, is compared to the approved product and its indicated use in the table below.

Patent Claim	Approved Product
11. A method of treating central nervous system disorders in an animal comprising administering to said animal in need thereof an anticonvulsant effective amount of a compound according to any one of claims 1-9.	The active ingredient of the approved product is lacosamide, and lacosamide falls within the scope of claim 1 as indicated above. Lacosamide is an anticonvulsant approved for the treatment of partial-onset seizures in patients with epilepsy, which is a central nervous system disorder.

10. A Statement, Beginning On A New Page, Of The Relevant Dates And Information Pursuant To 35 U.S.C. § 156(g) In Order To Enable The Secretary Of Agriculture, As Appropriate, To Determine The Applicable Regulatory Review Period As Follows (i): For A Patent Claiming A Human Drug Product, Antibiotic, Or Human Biological Product, The Effective Date Of The Investigational New Drug (IND) Application And The IND Number; The Date On Which A New Drug Application (NDA) Or A Product License Application (PLA) Was Initially Submitted And The NDA Or PLA Number And The Date On Which The NDA Was Approved Or The Product License Issued

The FDA via teleconference on May 19, 1999 advised that the IND for VIMPAT[®] tablet (IND 57,939) became effective on May 19, 1999. For purposes of this application for patent term extension, the Applicant is entitled to an IND date of at least as early as May 19, 1999. The NDA (NDA 22-253) for VIMPAT[®] tablet was initially submitted to the Food and Drug Administration on September 28, 2007 and was approved on October 28, 2008.

11. A Brief Description Beginning On A New Page Of The Significant Activities Undertaken By The Marketing Applicant During The Applicable Regulatory Review Period With Respect To The Approved Product And The Significant Dates Applicable To Such Activities

A brief description of significant activities undertaken by the marketing applicant during the regulatory review period with respect to the approved product is annexed as **Exhibit F**. This exhibit provides a chronology of the major communications between the marketing applicant and the Food and Drug Administration, including a brief summary of the subject matter and date of these communications.

Applicant reserves the right to supplement the chronology of **Exhibit F** with materials from which it was derived or other evidence related to Applicant's conduct in obtaining the approval of VIMPAT[®] tablet. *See, e.g.*, 21 CFR § 60.32.

12. A Statement Beginning On A New Page That In The Opinion Of The Applicant The Patent Is Eligible For The Extension And A Statement As To The Length Of The Extension Claimed, Including How The Length Of Extension Was Determined

Applicant is of the opinion that U.S. Patent No. Re38,551 is eligible for extension under 35 U.S.C. § 156, because it satisfies all of the requirements for such extension as follows:

- a. 35 U.S.C. §156(a); 37 CFR §1.720(a)
U.S. Patent No. Re38,551 claims a product, and a method of using a product.
- b. 35 U.S.C. §156(a)(1); 37 CFR §1.720(g)
The term of U.S. Patent No. Re38,551 has not expired before submission of this application.
- c. 35 U.S.C. §156(a)(2); 37 CFR §1.720(b)
The term of U.S. Patent No. Re38,551 has never previously been extended under 35 U.S.C. §156.
- d. 35 U.S.C. §156(a)(3); 37 CFR §1.730
This application for extension is submitted by the authorized agent or the owner of record in accordance with the requirement of 35 U.S.C. §156(d) and the rules of the U.S. Patent and Trademark Office.
- e. 35 U.S.C. §156(a)(4); 37 CFR §1.720(d)
The product VIMPAT® tablet has been subject to a regulatory review period as defined in 35 U.S.C. §156(g) before its commercial marketing or use.

f. 35 U.S.C. §156(a)(5)(A); 37 CFR §1.720(e)(i)

The commercial marketing or use of the product VIMPAT[®] tablet after the regulatory review period is the first permitted commercial marketing or use of the product under the provision of the Federal Food, Drug, and Cosmetics Act (21 U.S.C. §360) under which such regulatory review period occurred.

g. 35 U.S.C. §156(c)(4); 37 CFR §1.720(h)

No other patent has been extended for the same regulatory review period for the product VIMPAT[®] tablet.

h. 35 U.S.C. §156(d)(1); 37 CFR §1.720(f)

This application is submitted within the permitted 60 day period beginning on the date the product first received permission for commercial marketing or use.

Applicant is of the opinion that U.S. Patent No. Re38,551 is eligible for extension under 35 U.S.C. § 156 for 5 years, or 1827 days, as determined pursuant to 37 CFR §1.775 as follows:

Patent Information:

Patent 5,773,475 Issue Date	June 30, 1998
Earliest non-provisional priority date	March 17, 1997
Days Extension under 35 U.S.C. 154(b)	0

FDA Information:

Date IND Becomes Effective	May 19, 1999
Date NDA Submitted to the FDA	September 28, 2007
Date NDA Approved by the FDA	October 28, 2008

IND Period:

Start Date of Regulatory Review Period	May 19, 1999
IND Review Period (days)	3054
½ IND Review Period (days)	1527

Regulatory Review Period Allowed:

NDA Review Period (days)	397
Regulatory Review Period (days)	3451
Reg. Rev. Period less ½ IND period (days)	1924

Statutory Limitations:

Patent Expiration Date (20 year term)	March 17, 2017
Expiration under 5 year extension limitation (Date 1)	March 17, 2022
Expiration under 14 from NDA approval limitation (Date 2)	October 28, 2022
Expiration based upon full review period (Date 3)	June 23, 2022
Final Expiration Date (Earliest of Date 1, Date 2, or Date 3)	March 17, 2022
<u>Maximum Extension in Days:</u>	1827

13. A Statement That Applicant Acknowledges A Duty To Disclose To The Commissioner Of Patents And Trademarks And The Secretary Of Health And Human Services Any Information Which Is Material To The Determination Of Entitlement To The Extension Sought

Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to any determinations of entitlement to the extension sought in the Application.

14. The Prescribed Fee For Receiving And Acting Upon The Application For Extension

The prescribed fee pursuant to 37 CFR §1.20(j) for receiving and acting upon this application is to be charged to the Deposit Account of Applicant's undersigned attorney as authorized in the attached letter.

15. The Name, Address, And Telephone Number Of The Person To Whom Inquiries And Correspondence Relating To The Application For Patent Term Extension Are To Be Directed

Please address all correspondence to:

Kevin G. Shaw
Hogan & Hartson, LLP
555 Thirteenth St., NW
Washington, DC 20004

16. A Duplicate Of The Application Papers, Certified As Such

Applicant hereby certifies that this application for extension is being filed in triplicate.

17. An Oath Or Declaration

Applicant, through its undersigned patent attorney authorized to practice before the Patent and Trademark Office and who has general authority from the agent or owner to act on behalf of the agent or owner in patent matters, being duly warned that willful false statements are punishable by fine or imprisonment or both under section 1001 of Title 18, United States Code and that willful false statements and the like may jeopardize the validity of this application and the patent to which it relates, states and declares that the following statements made based on his own knowledge are true and that all statements made on information and belief are believed to be true:

- (1) The undersigned is registered to practice before the Patent and Trademark Office and is making this declaration as a patent attorney who has general authority to act on behalf of the applicant in patent matters.
- (2) The undersigned has reviewed and understands the contents of the application being submitted pursuant to this section;
- (3) The undersigned believes the patent is subject to an extension pursuant to 37 C.F.R. § 1.710 in the event of NDA approval and, in the interim, is subject to an extension pursuant to 37 C.F.R. § 1.790;
- (4) The undersigned believes an extension of the length claimed is justified under 35 U.S.C. 156 and the applicable regulations; and
- (5) The undersigned believes the patent for which extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 C.F.R. § 1.720 in the event of NDA approval, and meets the requirements for an interim extension of a patent set forth in 37 C.F.R. § 1.790.

If this application for extension of patent term is held to be informal, applicant may seek to have that holding reviewed by filing a petition with the required fee, as necessary, pursuant to 37 C.F.R. §§ 1.181, 1.182 or 1.183, as appropriate, within such time as may be set in any notice that the application has been held to be informal, or if no time is set, within one month of the date on which the application was held informal.

Respectfully submitted,

Dated: December 23, 2008

HOGAN & HARTSON LLP
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Customer No.: 24633

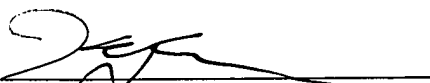
By: 
Kevin G. Shaw
Registration No. 43,110

Exhibit A

Exhibit B

LETTER OF RELIANCE

SCHWARZ
P H A R M A
A member of the UCB Group, Inc.

**Mail Stop Hatch-Waxman PTE
Office of Patent Legal Administration
Room MDW 7D55
600 Dulany Street (Madison Building)
Alexandria, VA 22314**

**Attn: Mary C. Till, Examiner
Office of Patent Legal Administration**

Schwarz Biosciences, Inc. (having its registered office at 1209, Orange Street, Wilmington, Delaware 19801, USA; "SBI") is directly held by UCB Inc. (having its registered office at 1209, Orange Street, Wilmington, Delaware 19801, USA), the latter being a directly and indirectly wholly-owned subsidiary of UCB Holdings, Inc. (having its registered office at 1209, Orange Street, Wilmington, Delaware 19801, USA) which is directly wholly-owned subsidiary of UCB S.A. (having its registered office at Allée de la Recherche 60, 1070 Brussels, Belgium).

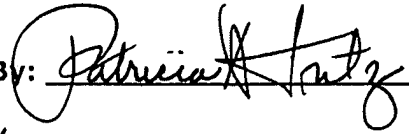
Schwarz Pharma AG (having its registered office at Alfred-Nobel Strasse 10, 40789 Monheim, Germany; "SPAG") is directly held by UCB SP GmbH (having an office at Alfred-Nobel Strasse 10, 40789 Monheim, Germany) which is a directly wholly-owned subsidiary of UCB GmbH (having its registered office at Alfred-Nobel Strasse 10, 40789 Monheim, Germany), the latter being directly and indirectly held by UCB S.A. (having its registered office at Allée de la Recherche 60, 1070 Brussels, Belgium).

SPAG has exclusive license rights regarding lacosamide, R-2-Acetamido-N-benzyl-3-methoxypropionamide, under U.S. Patent Nos. Re38,551 and 5,654,301, as sublicensee of Harris FRC Corporation (having an office at 2137 Route 35 Holmdel, New Jersey 07733; "Harris FRC") that is licensee from Research Corporation Technologies, Inc. (having an office at 5210 E. Williams Circle, Suite 240, Tucson, Arizona 85711-4410; "RCT"). Hence, SPAG, Harris FRC, and RCT are sublicensee, licensee and assignee, respectively, of U.S. Patent Nos. Re38,551 and 5,654,301.

SBI, as NDA holder, authorizes RCT to rely on activities of SBI and its predecessors in interest relating to FDA approval of VIMPAT® lacosamide products as adjunctive therapy in treatment of partial-onset seizures in patients with epilepsy, in Tablet form under NDA 22-253 and in Injection form under NDA 22-254, in support of RCT's intension to apply for extension of patent term of U.S. Patent Nos. Re38,551 and 5,654,301, as provided under 35 U.S.C. §156(d) (1), 37 C.F.R. §1.730 and MPEP 2752.

SCHWARZ
P H A R M A

Authorized by Schwarz Biosciences, Inc.

By: 

Date: 12-01-08

for
Deborah Hogerman
Senior Director, U.S. Regulatory Affairs
On behalf of Schwarz Biosciences, Inc.

cc: Research Corporation Technologies, Inc.
cc: Harris FRC Corporation

Exhibit C



NDA APPROVAL

NDA 22-253

NDA 22-254

Schwarz Biosciences, Inc.
Attention: Alan Blumberg
Senior Director, US Regulatory Affairs
P.O. Box 110167
Research Triangle Park, NC 27709

Dear Mr. Blumberg:

Please refer to your new drug applications (NDAs) dated September 28, 2007, received September 28, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Vimpat (lacosamide) Tablets, 50 mg, 100 mg, 150 mg, and 200 mg, and Vimpat (lacosamide) Injection, 200 mg per 20 ml.

We acknowledge receipt of your additional submissions dated:

November 26, 2007	March 20, 2008	April 30, 2008	July 17, 2008	September 4, 2008
December 13, 2007	April 3, 2008	May 9, 2008	July 30, 2008	September 23, 2008
January 23, 2008	April 9, 2008	May 27, 2008	August 1, 2008	October 15, 2008
February 13, 2008	April 14, 2008	June 11, 2008	August 14, 2008	October 21, 2008
February 22, 2008	April 18, 2008	July 11, 2008 (2)	August 27, 2008	

These new drug applications provide for the use of Vimpat (lacosamide) as follows:

- Vimpat (lacosamide) Tablets as adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older.
- Vimpat (lacosamide) Injection as adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older when oral administration is temporarily not feasible.

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

Your applications for Vimpat (lacosamide) Tablets and Injection (NDA 22-253, 22-254) were not referred to an FDA advisory committee because your products are members of the class of previously approved anti-epileptic drugs and the products did not pose unique concerns beyond those applicable to other members of this class.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 1 month for these applications because necessary studies are impossible or highly impracticable because there are too few children with partial onset seizures in this age group to study.

In addition, we are deferring submission of your pediatric studies in partial onset seizures for ages 1 month up to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

1. Deferred pediatric studies under PREA for the adjunctive treatment of partial onset seizures in pediatric patients ages 1 month up to 17 years.

Final Report Submission: July 2013

Submit final study reports to these NDAs. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated “**Required Pediatric Assessment.**”

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

Title IX, Subtitle A, Section 901 of Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Vimpat (lacosamide) poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is

necessary for patients' safe and effective use of Vimpat (lacosamide). FDA has determined that Vimpat (lacosamide) has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use Vimpat (lacosamide). In addition, patient labeling could help prevent serious adverse effects related to the use of these products. Vimpat (lacosamide) may increase the risk of suicidal thoughts or behavior in patients taking anti-epileptic drugs for any indication. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Vimpat (lacosamide).

Your proposed REMS, submitted on October 17, 2008, in an electronic communication, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your October 17, 2008 submission.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

- **NDA 22-253 & 22-254 REMS ASSESSMENT**
- **NEW SUPPLEMENT FOR NDA 22-253 & 22-254**
PROPOSED REMS MODIFICATION
< other supplement identification > [if included]
<REMS ASSESSMENT> [if included]

POSTMARKETING REQUIREMENTS UNDER 505(o)

Title IX, Subtitle A, Section 901 of FDAAA amends the FDCA to authorize FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the known serious risk of developmental neurotoxicity.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) has not yet been established and is not sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required, pursuant to section 505(o)(3) of the FDCA, to conduct the following study:

2. A nonclinical study in rats to examine the effects of Vimpat (lacosamide) on brain development during the prenatal and early postnatal periods using more sensitive techniques for assessing central nervous system structure and function than were employed in the standard pre- and postnatal development study. You should consider the use of multiple daily dosing as a means of achieving higher plasma drug exposures during pregnancy and to better mimic the human exposure pattern.

The timetable you have submitted on October 28, 2008 states that you will conduct this study according to the following schedule:

Protocol Submission:	Within 6 months of approval
Final Report Submission:	Within 30 months of approval

Submit protocols to your IND 57,939 with a cross-reference letter to these new drug applications (NDA) 22-253 and 22-254. Submit final reports to your NDAs 22-253 and 22-254. Please use the following designators to label prominently all submissions, including supplements, relating to this postmarketing study as appropriate:

- **Required Postmarketing Protocol under 505(o)**
- **Required Postmarketing Final Report under 505(o)**
- **Required Postmarketing Correspondence under 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS

We acknowledge your written commitment to conduct the following postmarketing study as described in your submission dated October 28, 2008, as outlined below:

3. *In vitro* data to determine which enzymes may be involved in the metabolism of Vimpat (lacosamide) in addition to CYP2C19.

Final Report Submission: within 18 months of approval

Submit the protocol to your IND (b)(5)(4). Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to these NDAs. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to these NDAs. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study.

All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled:

- **Postmarketing Study Commitment Protocol**
- **Postmarketing Study Commitment Final Report**
- **Postmarketing Study Commitment Correspondence**

HIGHLIGHTS WAIVER

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

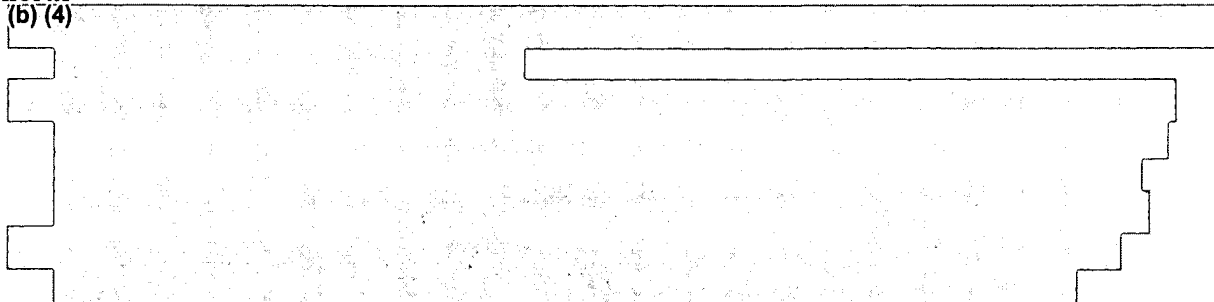
As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert and Medication Guide). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, **“SPL for approved NDA 22-253 and NDA 22-254.”**

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission **“Final Printed Carton and Container Labels for approved NDA 22-253 and NDA 22-254”** Approval of this submission by FDA is not required before the labeling is used.

In addition, we note your agreement on October 28, 2008 to address and make the following changes into your carton and immediate container labels:

General **(b) (4)**



[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

(b) (4)

[REDACTED]

(b) (4)

[REDACTED]

(b) (4)



Marketing the products with FPL that is not identical to the approved labeling text including the changes noted above may render the product misbranded and an unapproved new drug.

CONTROLLED SUBSTANCE CLASS

We have recommended that this product be scheduled under the Controlled Substances Act. We remind you of the following statement that appears on the Form FDA 356h, "If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision." Once a final scheduling decision is made, your label must be amended to reflect the schedule.

EXPIRATION DATE (Injection)

We grant the proposed 36 month drug product expiry, when stored at controlled room temperature, for lacosamide 200 mg/20 mL injection packaged in 20 mL type I colorless glass vials with a grey rubber stopper coated with a (b) (4) and aluminum overseal.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Jacqueline H. Ware, Pharm.D., Supervisory Regulatory Project Manager, at (301) 796-1160.

Sincerely,

{See appended electronic signature page}

Ellis F. Unger, M.D.
Deputy Director (Acting)
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures (FDA Approved Labeling Text, Medication Guide, and REMS document)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Ellis Unger
10/28/2008 08:00:13 PM

Exhibit D



US00RE38551E1

(19) **United States**
 (12) **Reissued Patent**
Kohn

(10) **Patent Number:** **US RE38,551 E**
 (45) **Date of Reissued Patent:** **Jul. 6, 2004**

(54) **ANTICONVULSANT ENANTIOMERIC
 AMINO ACID DERIVATIVES**

(75) **Inventor:** **Harold Kohn**, Chapel Hill, NC (US)

(73) **Assignee:** **Research Corporation Technologies,
 Inc.**, Tucson, AZ (US)

(21) **Appl. No.:** **10/058,634**

(22) **Filed:** **Jan. 28, 2002**

Related U.S. Patent Documents

Reissue of:

(64) **Patent No.:** **5,773,475**
Issued: **Jun. 30, 1998**
Appl. No.: **08/818,688**
Filed: **Mar. 17, 1997**

U.S. Applications:

(60) **Provisional application No.** 60/013,522, filed on Mar. 15, 1996.

(51) **Int. Cl.⁷** **A61K 31/165; C07C 233/05**

(52) **U.S. Cl.** **514/616; 564/155; 564/158**

(58) **Field of Search** **514/616; 564/155,
 564/158**

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,378,729 A 1/1995 Kohn et al. 514/231.2
 5,654,301 A 8/1997 Kohn et al. 514/231.2

FOREIGN PATENT DOCUMENTS

EP 0 194 464 9/1986

OTHER PUBLICATIONS

Anderson, et al. *J. Am. Chem. Soc.* 89:19 pp. 5012-5017, (1967).

Kohn, Harold, et al. "Preparation and anticonvulsant activity of a series of functionalized. alph.-heteroatom-substituted amino acids", *J. Med. Chem.* 34, 2444-2452 (1991).

Kohn, Harold, et al. "Marked stereospecificity in a new class of anticonvulsants", *Chemical Abstracts*, 109 (1988) Abstract No. 183045.

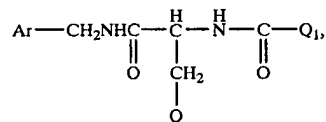
Choi, Daeock, et al. "Synthesis and Anticonvulsant Activities of N-Benzyl-2-acetamidopropionamide Derivatives", *J. Med. Chem.*, 39: 1907-1916 (1996).

Primary Examiner—Shailendra Kumar

(74) *Attorney, Agent, or Firm*—Scully, Scott, Murphy & Presser

(57) **ABSTRACT**

The present invention is directed to a compound in the R configuration about the asymmetric carbon in the following formula:



pharmaceutical compositions containing same and the use thereof in treating CNS disorders in animals.

13 Claims, No Drawings

Exhibit E



Customer No 124

ISTMT

DATE PRINTED
11/19/2008

MASTER DATA CENTER, INC.
29100 NORTHWESTERN HIGHWAY
SUITE 300
SOUTHFIELD MI 48034-1095

MAINTENANCE FEE STATEMENT

According to the records of the U.S. Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O. Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,773,475	\$850.00	\$0.00	09/28/01	08/818,688	06/30/98	03/17/97	04	NO	10030



Customer No 124

ISTMT

DATE PRINTED
11/21/2008MASTER DATA CENTER, INC.
29100 NORTHWESTERN HIGHWAY
SUITE 300
SOUTHFIELD MI 48034-1095

MAINTENANCE FEE STATEMENT

According to the records of the U.S. Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O. Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
RE38,551	\$2,300.00	\$0.00	11/23/05	10/058,634	06/30/98	03/17/97	08	NO	RE10030I

Exhibit F

Exhibit F

A brief description of significant activities undertaken by the sponsor, Schwarz Biosciences, Inc. ("Schwarz") (or its predecessor in interest), during the regulatory review period for VIMPAT® (lacosamide) tablets, together with applicable dates, follows below.

1. Overview

Between May 19, 1999 and September 28, 2007, Schwarz conducted multiple clinical studies of VIMPAT® using the tablet formulation, including three primary, multicenter, double-blind, randomized, placebo-controlled, parallel-group studies, 1 completed open-label, supporting efficacy study, and 3 ongoing open-label extension studies evaluating long-term safety and efficacy. Two additional completed open-label studies used a capsule formulation. Schwarz also conducted at least 13 pharmacokinetic and pharmacodynamic studies.

Between September 28, 2007 and October 28, 2008, Schwarz responded to numerous requests for information from FDA. The dates of those responses are summarized in Section 4.

2. Key Regulatory Dates

February 22, 1999	IND 57,939 submitted to FDA
March 24, 1999	Teleconference with FDA – FDA informed that IND is on clinical hold
May 19, 1999	Teleconference with FDA - FDA informed that IND is in effect
May 12, 2000	Notification to FDA (via letter) of transfer of sponsorship of IND 57,939 from Harris FRC Corporation to Schwarz
June 9, 2000	FDA acknowledgment of transfer
November 3, 2004	End-of-Phase II Meeting with FDA
July 19, 2006	Pre-NDA Meeting with FDA
September 6, 2006	Meeting with FDA regarding abuse liability
September 28, 2007	NDA 22-253 submitted to FDA
October 22, 2007	FDA letter acknowledging receipt of NDA
December 10, 2007	FDA letter accepting NDA for filing
October 28, 2008	FDA approval letter of NDA 22-253

3. Summary of Phase III Clinical Studies

Start	Stop	Study
FSI 11 Feb 2002	LSO 07 May 2004	SP667 (multicenter, double-blind, randomized, placebo-controlled parallel group study to investigate efficacy and safety of adjunctive therapy in subjects with partial seizures with or without secondary generalization)
FSI 07 Jun 2004	LSO 24 Jan 2006	SP755 (multicenter, double-blind, randomized, placebo-controlled parallel group study to investigate efficacy and safety of adjunctive therapy in subjects with partial seizures with or without secondary generalization)
FSI 18 Mar 2004	LSO 16 Aug 2006	SP754 (multicenter, double-blind, randomized, placebo-controlled parallel group study to investigate efficacy and safety of adjunctive therapy in subjects with partial seizures with or without secondary generalization)

4. NDA Amendments

Following the initial submission of the NDA on September 28, 2007, Schwarz submitted additional information to FDA on the following dates:

November 26, 2007	April 14, 2008	July 30, 2008
December 13, 2007	April 18, 2008	August 1, 2008
January 23, 2008	April 30, 2008	August 14, 2008
February 13, 2008	May 9, 2008	August 27, 2008
February 22, 2008	May 27, 2008	September 4, 2008
March 20, 2008	June 11, 2008	September 23, 2008
April 3, 2008	July 11, 2008 (2)	October 15, 2008
April 9, 2008	July 17, 2008	October 21, 2008

5. Additional Information

A more detailed description of the activities undertaken by the NDA holder, including those otherwise listed above in this Exhibit, is set forth in the IND 57,939 Submissions and NDA 22-253 Submissions tables (each table being produced across multiple pages that are independently numbered) produced on the remainder of the pages of this Exhibit.

IND 57,939 Submissions

Submission Date	Serial No	Location	Submission Type	Study No	Title/ Description	CIOMS	
						Mfr Control No	Subject No
22-Feb-99	000	V1 P0029	Initial IND		Item 3: Introductory Statement		
22-Feb-99	000	V1 P0034	Initial IND		Item 4: General Investigational Plan		
22-Feb-99	000	V1 P0040	Initial IND		Item 5: Investigator's Brochure		
22-Feb-99	000	V1 P0337	Initial IND		Investigator Data		
22-Feb-99	000	v10 p0001	Initial IND	148-235	13-Week Oral Gavage Subchronic Toxicity Study of ADD 234037 in Rats		
22-Feb-99	000	V10 P0001	Initial IND	148-235	13-Week Oral Gavage Subchronic Toxicity Study of ADD 234037 in Rats		
22-Feb-99	000	v12 p0001	Initial IND	98793	14-Day Intravenous Injection Toxicity Study of ADD 234037 in Beagle Dogs		
22-Feb-99	000	V12 P0001	Initial IND	98793	14-Day Intravenous Injection Toxicity Study of ADD 234037 in Beagle dogs		
22-Feb-99	000	V12 P0162	Initial IND	6842-102	Three Day Toxicity Study of Orally Administered ADD 234037 in Dogs (Abbreviated Report)		
22-Feb-99	000	v12 p0162	Initial IND	6842-102	Three Day Toxicity Study of Orally Administered ADD 234037 in Dogs		
22-Feb-99	000	V12 P0164	Initial IND	98825	30-Day Oral Toxicity Study of ADD 234037 in Beagle Dogs		

Monday, November 10, 2008

IND 57,939

Page 1 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
22-Feb-99	000	v12 p0164	Initial IND	98825	30-Day Oral Toxicity Study of ADD 234037 in Beagle Dogs		
22-Feb-99	000	v13 p0001	Initial IND	G94BR23.502	Bacterial Reverse Nyrtatuib Assay		
22-Feb-99	000	V13 P0001	Initial IND	G97BR23.502	Bacterial Reverse Mutation Assay		
22-Feb-99	000	V13 P0045	Initial IND	G97BR23.704	In Vitro Mammalian Cell Gene Mutation Test		
22-Feb-99	000	v13 p0045	Initial IND	G97BR12.704	In Vitro Mammalian Cell Gene Mutation Test		
22-Feb-99	000	V13 P0084	Initial IND	G97BR23.123	Mammalian Erythrocyte Micronucleus Test		
22-Feb-99	000	v13 p084	Initial IND	G97BR23.123	Mammalian Erythrocyte Micronucleus Test		
22-Feb-99	000	v14 p0001	Initial IND	Previous Human E			
22-Feb-99	000	V14 P0001	Initial IND	Item 9: Previous Human Experience			
22-Feb-99	000	v14 p0016	Information Amendment: Clinical	Additional Infor			
22-Feb-99	000	V14 P0016	Initial IND	Item 10: Additional Information			

Monday, November 10, 2008

IND 57,939

Page 2 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
22-Feb-99	000	V2 P0001	Initial IND	FRC 01-201	Item 6: A Phase II Multicenter, Ascending Dose Assessment of the Safety, Tolerability, Compatibility, Efficacy and Pharmacokinetics of Harkoseride (ADD 234037) as Adjunctive Therapy in Patients with Partial Seizures		
22-Feb-99	000	V3 P0001	Initial IND		Item 7: Chemistry, Manufacturing and Control Data		
22-Feb-99	000	V4 P0001	Initial IND		Item 8: Pharmacology and Toxicology Information		
22-Feb-99	000	V4 P0081	Initial IND	A2	Thirty-Seven Receptor Binding Assays (Summary)		
22-Feb-99	000	V4 P0141	Initial IND	A3	Biochemical Assay Reports on ADD 234037: Glutamate and NMDA Glycine Receptor Binding (Summary)		
22-Feb-99	000	V4 P0173	Initial IND	Wasterlain 1	Determination of the Relative Affinity of ADD 234037 for the Glycine Binding Site of Rat Brain NMDA Receptor		
22-Feb-99	000	V4 P0180	Initial IND	A4	D-Serine Reversal of ADD 234037		
22-Feb-99	000	V4 P0182	Initial IND	N01-NS-4-2311	The Profile of Anticonvulsant Activity and Minimal Toxicity of ADD 234037 in Mice and Rats (Kupferberg H. J. et al.)		
22-Feb-99	000	V4 P0217	Initial IND	A5	Effects of Harkoseride in NIE-115 Neuroblastoma Cells (Summary)		

Monday, November 10, 2008

IND 57,939

Page 3 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS</i>	
						<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
22-Feb-99	000	V4 P0231	Initial IND	Wasterlain 2	The Effects of ADD 234037 and Fosphenytoin on Self-Sustaining Status Epilepticus Induced in Rats by Brief Intermittent Perforant Path Stimulation		
22-Feb-99	000	V4 P0240	Initial IND	Wasterlain 3	The Effects of ADD 234037 on Hippocampal Damage from Status Epilepticus Induced in Rats by Perforant Path Stimulation		
22-Feb-99	000	V4 P0245	Initial IND	Wasterlain 4	The Effects of ADD 234037, Diazepam and Phenytoin on Self-Sustaining Status Epilepticus Induced in Rats by Intermittent Perforant Path Stimulation		
22-Feb-99	000	V5 P0001	Initial IND	A1	Efficacy of Harkoseride in Rat Models of Chemically Induced Self-Sustaining Status Epilepticus: Monotherapy or in Combination with Diazepam		
22-Feb-99	000	V5 P0023	Initial IND	DS Panlabs MCA	Brain ischemia: Effects of ADD 234037 on Permanent Focal Ischemia in Rats Via Middle Cerebral Artery Occlusion (MCAO)		
22-Feb-99	000	V5 P0042	Initial IND	A7	The Efficacy of ADD 234037 in Treating Focal Ischemia (MCAO) in Rats		
22-Feb-99	000	V5 P0115	Initial IND	0200XH15.001	Neuropharmacological Profile (NPP) in Mice		
22-Feb-99	000	V5 P0130	Initial IND	A6	Report on In Vitro Carbonic Anhydrase Inhibition, Change in Heart Rate and Blood Pressure in Spontaneously Hypertensive Rats, and Saluresis/Kaluresis in Normal Rats		

Monday, November 10, 2008

IND 57,939

Page 4 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>		<i>Title/ Description</i>		<i>CIOMS</i>		<i>CIOMS</i>
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>					<i>Mfr Control No</i>		<i>Subject No</i>
22-Feb-99	000	V5 P0150	Initial IND	A8		The effects of ADD 234037 on the Transmembrane Potentials of Isolated Canine Ventricular Myocytes (Hoffmann B. F.)				
22-Feb-99	000	V5 P0152	Initial IND	0234DH15.001		Pharmacodynamic Assay of ADD 234037 in Dogs (Gromelski G. J. and Ciofalo V. B.)				
22-Feb-99	000	V5 P0161	Initial IND	0234DH15.002		Pharmacodynamic (Autonomic) Assay of ADD 234037 in Dogs (Gromelski G. J., Gayheart-Walsten P.)				
22-Feb-99	000	V6 P0001	Initial IND	0247DH15.003		Cardiovascular Evaluation of ADD 234037 in a Dog (Gayheart-Walsten P., Gromelski B. S.)				
22-Feb-99	000	V6 P0028	Initial IND	0247DH15.001		Cardiovascular (hemodynamic) evaluation of ADD 234037 in the open-chest anesthetized dog				
22-Feb-99	000	V6 P0038	Initial IND	0247DH15.002		Cardiovascular (Hemodynamic) Evaluation of ADD 234037 in Dogs				
22-Feb-99	000	V6 P0064	Initial IND	0247XH15.004		Cardiovascular Evaluation of ADD 234037 in Non-Human Primates				
22-Feb-99	000	V6 P102	Initial IND	Gordon (MDS)		LC-MS/MS Method Development and the Determination of Concentration Levels of Compound ADD 234037 in Rat Plasma (Gordon W. P.)				
22-Feb-99	000	V6 P151	Initial IND			Determination of Concentration Levels of ADD 234037 in Rat Plasma (Taylor L. C., Gordon W. P., Kobel, M.)				

Monday, November 10, 2008

IND 57,939

Page 5 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
22-Feb-99	000	V7 P0001	Initial IND	AV-0005	Assay Validation Report: LC-MS/MS Assay of ADD 234037 (Gordon W. P.)		
22-Feb-99	000	V7 P0094	Initial IND	Walton	Pharmacokinetics and Protein Binding of ADD 234037 in the Rat (Memo)		
22-Feb-99	000	V7 P0097	Initial IND	18566-0-800	Acute IV Study of ADD 234037 in Rats		
22-Feb-99	000	V7 P0111	Initial IND	6842-100	Rising Dose Tolerance Intravenous Injection Toxicity Study of ADD 234037 in Dogs		
22-Feb-99	000	V7 P0189	Initial IND	6842-103	Rising Dose Tolerance Oral (Capsule) Toxicity Study of ADD 234037 in Dogs		
22-Feb-99	000	V8 P0001	Initial IND	6842-101	14-Day Intravenous Injection Toxicity Study of ADD 234037 in Rats		
22-Feb-99	000	V9 P0001	Initial IND	CHV 148-234	30-Day Range-Finding Oral Toxicity Study of ADD 234037 in Rats		
24-Feb-99			NA		FRC provides 12 additional copies of V1 from the initial IND		
25-Feb-99			FDA Phone Contact		Ms. Chen, FDA contacted Mr. Ostroff, FRC for 12 additional copies of V1 of the IND		
26-Feb-99			FDA Correspondence		Acknowledgement of IND		
12-Mar-99			FDA Correspondence		FDA letter containing CMC reviewer comments		

Monday, November 10, 2008

IND 57,939

Page 6 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
12-Mar-99			FDA Phone Contact		Ms. Chen, FDA contacted Mr. Ostroff, FRC regarding CMC reviewer comments		
15-Mar-99			FDA Phone Contact		Telecon between Dr. Harris, FRC, Dr. Broadbent, FDA, and Mr. Ostroff, FRC regarding CMC issues		
16-Mar-99			FDA Meeting Minutes		Minutes from 15-mar-99 telecon		
16-Mar-99			NA		Dr. Lukas, FRC faxed FDA phone contact report regarding comments from 15-mar-99 telecon to Dr. Broadbent, FDA		
18-Mar-99			NA		Dr. Lukas, FRC provided requested CMC information to Dr. Broadbent, FDA. Unofficial Correspondence.		
18-Mar-99			FDA Phone Contact		Ms. Chen, FDA requested telecon to discuss clinical issues		
18-Mar-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Chen, FDA to schedule clinical telecon		
18-Mar-99			FDA Correspondence		FDA letter containing medical reviewer comments		
20-Mar-99			NA		Dr. Lukas, FRC provided requested CMC information to Dr. Broadbent, FDA. Unofficial Correspondence.		
22-Mar-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Chen, FDA to confirm telecon on 24-mar-99		

Monday, November 10, 2008

IND 57,939

Page 7 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
24-Mar-99			FDA Meeting Minutes		Minutes from the telecon held between Dr. Katz, FDA, and FRC. IND placed on clinical hold		
30-Mar-99			FDA Phone Contact		Dr. Harris, FRC contacted Dr. Katz, FDA to discuss clinical hold		
31-Mar-99			FDA Correspondence		FDA Letter stating IND placed on clinical hold		
21-Apr-99	001		Response to Clinical Hold	FRC 01-201	Provided revised protocol addressing FDA concerns		
17-May-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Chen, FDA to schedule telecon to discuss preclinical issues and comments from FDA clinical hold letter dated 31-mar-99.		
19-May-99			FDA Phone Contact		Ms. Malandrucchio, FDA contacted Mr. Ostroff, FRC regarding clinical hold. The IND is released from clinical hold.		
19-May-99	002		Response to Clinical Hold		Commitment from FRC to obtain additional standard 12-lead electrocardiogram on all patients receiving 300mg bid dose		
22-Jun-99	003		Protocol Amendment: New Investigator				
22-Jun-99	004		Response to FDA Request for Information		Response to FDA letter dated 31-mar-99		

Monday, November 10, 2008

IND 57,939

Page 8 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
08-Jul-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Malandruccho, FDA to discuss status of review Response to Clinical Hold dated 22-jun-99 SN 004. Mr. Nighswander, FDA was contacted. He suggested providing a formal meeting request package for a telecon to discuss issues.		
09-Jul-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Mr. Nighswander, FDA to inquire on status of review of Response to Clinical Hold submitted 22-jun-99 SN 004. No response available.		
12-Jul-99			FDA Phone Contact		Dr. Broadbent, FDA contacted Mr. Ostroff, FRC regarding impurity identification and request for monthly stability updates for Lot KJ01946.		
15-Jul-99			NA		FRC fax to Dr. Broadbent, FDA containing stability updates for Lot KJ01946. Unofficial correspondence.		
23-Jul-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Malandruccho, FDA regarding review status of Response to Clinical Hold submitted 22-jun-99 SN 004. Ms. Malandruccho stated a response would be provided as soon as possible.		
27-Jul-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Malandruccho, FDA to request a telecon to discuss the review of the Response to Clinical Hold dated 22-jun-99 SN 004. Ms. Malandruccho did not return Mr. Ostroff's call.		

Monday, November 10, 2008

IND 57,939

Page 9 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
27-Jul-99	005		Protocol Amendment: Change in Protocol	FRC 01-201	Amendment A		
29-Jul-99	006		Information Amendment: Chemistry, Manufacturing an		Stability update for Lot KJ01946		
30-Jul-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Dr. Broadbent, FDA regarding stability update to Lot KJ01946. Mr. Ostroff faxed Dr. Broadbent copy of submission dated 29-jul-00 SN 006.		
05-Aug-99			FDA Phone Contact		Ms. Malandrucchio, FDA contacted Mr. Ostroff, FRC to discuss Response to Clinical Hold letter dated 22-jun-99 SN 004, CMC issues, toxicology issues, revisions to IB.		
20-Aug-99			FDA Correspondence		FDA letter in response to FRC's Response to Clinical Hold letter dated 22-jun-99 SN 004 which addressed comments in FDA letter dated 31-mar-99.		
25-Aug-99			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Malandrucchio, FDA requesting a telecon to discuss the toxicology study suggested in FDA letter dated 8/20/99. FDA denied a telecon.		
28-Sep-99	007		Information Amendment: CMC Data		Stability update for Lot KJ01946		
08-Oct-99	008		Response to FDA Request for Information	G97BR23.123	Mammalian Erythrocyte Micronucleus Test		

Monday, November 10, 2008

IND 57,939

Page 10 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
08-Oct-99	008		Response to FDA Request for Information		Investigator's Brochure		
08-Oct-99	009		Protocol Amendment: New Investigator	FRC 01-202			
08-Oct-99	009		Protocol Amendment: New Protocol	FRC 01-202	Original protocol		
29-Nov-99	010		Information Amendment: Chemistry, Manufacturing an		Stability update for Lot KJ01946		
13-Dec-99	011		Information Amendment: Chemistry, Manufacturing an		Stability update for Lot KJ01946		
15-Dec-99	012		Protocol Amendment: New Investigator	FRC 01-202			
04-Jan-00	013		Initial Safety Report	FRC 01-201	Subject No. AWD/03007 experienced visual hallucinations		AWD/03007
05-Jan-00	014		Protocol Amendment: New Investigator	FRC 01-201			
13-Jan-00	015		Protocol Amendment: New Investigator	FRC 01-202			
07-Feb-00			FDA Phone Contact		Dr. Broadbent, FDA contacted Mr. Ostroff, FRC to relieve Harris of ongoing stability commitment for Lot KJ01946.		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
07-Feb-00			FDA Phone Contact		Mr. Ostroff, FRC contacted Ms. Malandrucchio, FDA regarding transfer of sponsorship of IND to Schwarz Pharma.		
15-Feb-00	016		Information Amendment: Chemistry, Manufacturing an		Stability update for Lot KJ01946		
22-Feb-00	017		Follow-up Safety Report	FRC 01-201	Subject No. AWD/03007 additional information concerning the visual hallucinations		AWD/03007
15-Mar-00	018		Information Amendment: Clinical	FRC 01-202	Request to re-enroll Dr. Fountain's patient CDM		
16-Mar-00			FDA Phone Contact	FRC 202	Mr. Ostroff, FRC contacted Mr. Nighswander, FDA to follow-up on request dated 15-mar-00 SN 018 to re-enroll Dr. Fountain's patient.		
20-Mar-00			FDA Phone Contact	FRC 202	Ms. Malandrucchio, FDA contacted Mr. Ostroff, FRC to approve re-enrollment of one patient should he experience significant exacerbation of seizures during down titration. Formal letter to follow.		
21-Mar-00			FDA Correspondence	FRC 202	FDA fax to approve re-enrollment of Dr. Fountain's patient. Longer term animal data will be required to continue patients further.		
27-Mar-00	019		Information Amendment: Clinical	FRC 01-202	Submission of additional information to support 15-mar-00 SN 018 request to re-enroll Dr. Fountain's patient CDM as well as additional patients.		

Monday, November 10, 2008

IND 57,939

Page 12 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>CIOMS</i>			<i>Mfr Control No</i>	<i>Subject No</i>
31-Mar-00			FDA Phone Contact		FRC 202	Mr. Ostroff, FRC contacted Ms. Malandruccho, FDA regarding re-enrollment request dated 27-mar-00 SN 019. Ms. Malandruccho stated request was approved but was vague under what terms. She stated a letter would be sent to clarify FDA concerns.		
05-Apr-00			FDA Phone Contact		FRC 202	Mr. Ostroff, FRC contacted Mr. Nighswander, FDA to follow-up on FDA internal meeting regarding 15-mar-00 SN 018 and 27-mar-00 SN 019 submissions.		
10-Apr-00			FDA Correspondence		FRC 202	FDA fax approving request of 27-mar-00 SN 019 to re-enroll 7 patients without down-titrating.		
10-Apr-00			FDA Phone Contact		FRC 202	Mr. Ostroff, FRC contacted Ms. Malandruccho, FDA regarding re-enrollment request of 27-mar-00 SN 019. Ms. Malandruccho stated the memo on the meeting would be sent as soon as signed off on.		
12-May-00	020		Change of Sponsor			Transfer of application from FRC to Schwarz Pharma Inc.		
15-May-00	021		Change of Sponsor			Schwarz Pharma notification to FDA of acceptance of application		
09-Jun-00			FDA Correspondence			FDA acknowledgement letter of transfer of sponsorship.		

Monday, November 10, 2008

IND 57,939

Page 13 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
09-Jun-00			FDA Phone Contact		Mr. Foster, SB contacted Ms. Fanari, FDA to confirm transfer of sponsor and discuss neuropathic pain IND. Ms. Fanari stated a pilot study could be done under the current IND but the Div. of Analgesia would handle pain INDs.		
27-Jun-00	022		General Correspondence	FRC 01-202	Request to re-enroll three of Dr. Fountain's patients CDM, LRE, AWD		
30-Jun-00			FDA Phone Contact	FRC 202	Dr. Blumberg, SB contacted Ms. Fanari, FDA regarding 6/27/00 SN 022 submission to re-enroll 3 of Dr. Fountain's patients. FDA approved request but needs a minimum of 2 weeks notice for future requests.		
10-Jul-00			FDA Phone Contact	FRC 202	Mr. Foster and Dr. Blumberg, SB contacted Dr. Hershkowitz, FDA to discuss re-enrollment of Dr. Fountain's patients (6/27/00, SN 022). Topics: status of animal studies requested of Harris, Olney lesion study, additional ECGs requested.		
11-Jul-00	023	V1 P001	Information Amendment: Pharmacology/Toxicology	135293-ADD	Pharmacology Data Report: Evaluation of The Effects of ADD 234037 On Analgesia Acetic Acid Writhing, Formalin, Tail Flick, Anxiety, 5-MeODMT Potentiation And Glutamate NMDA Agonism/Antagonism Assay		
11-Jul-00	023	V1 P014	Information Amendment: Pharmacology/Toxicology	1108-005	One-Month Supplemental Range-Finding Toxicity Study of ADD 234037 in Rats		
11-Jul-00	023	V1 P086	Information Amendment: Pharmacology/Toxicology	98865	3-Month Oral Toxicity Study of ADD 234037 in Beagle Dogs		

Monday, November 10, 2008

IND 57,939

Page 14 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
11-Jul-00	023	V1 P299	Information Amendment: Pharmacology/Toxicology	9817552	Determination of Concentration Levels of ADD 234037 in Rat Plasma; Pharmacokinetic Evaluation Report		
11-Jul-00	023	V2 P001	Information Amendment: Pharmacology/Toxicology	9817555	Determination of Concentration Levels of ADD 234027 In Dog Plasma; Concentration And Pharmacokinetic Evaluation Report (Evaluation of the Pharmacokinetics of ADD 234037 In Male And Female Beagle Dogs Following An Escalation Oral Administration)		
11-Jul-00	023	V2 P071	Information Amendment: Pharmacology/Toxicology	9817551	Determination of Concentration Levels of ADD 234027 In Dog Plasma		
11-Jul-00	023	V2 P230	Information Amendment: Pharmacology/Toxicology	9825451	Determination of Concentration Levels of ADD 234037 In Dog Plasma		
11-Jul-00	023	V2 P387	Information Amendment: Pharmacology/Toxicology	98865BA	Quantitative Determination of ADD 234037 In Dog Plasma Specimens For Harris FRC Corporation		
11-Jul-00	023	V2 P405	Information Amendment: Pharmacology/Toxicology	98865PK	Determination of Concentration Levels of ADD 234037 in Dog Plasma; Toxicokinetic Evaluation Report (Evaluation of the toxicokinetics of ADD 234037 in Male and Female Beagle Dogs During Oral Administration for 3 Months)		
11-Jul-00	023	V3 P001	Information Amendment: Pharmacology/Toxicology	F212	Absorption, Distribution, Metabolism, And Excretion of [14C] ADD 234037 In Sprague Dawley Rats Following Either A Single Intravenous Or Oral Administration		
11-Jul-00	023	V3 P156	Information Amendment: Pharmacology/Toxicology	F232	Bioavailability And Excretion of [14C] ADD 234037 in Male Beagle Dogs Following Single Administration		

Monday, November 10, 2008

IND 57,939

Page 15 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
11-Jul-00	023	V3 P236	Information Amendment: Pharmacology/Toxicology	M1999-057	An Investigation of the Potential for Harkosende to Inhibit Cytochrome P450 1A2, 2A6, 2C9, 2C19, 2D6, 2E1, and 3A4 in Cryopreserved Human Hepatocytes		
11-Jul-00	023	V3 P254	Information Amendment: Pharmacology/Toxicology	9818851	In Vitro Metabolism of ADD 234037 Using Liver Microsomes From Rat, Dog, Monkey and Human		
11-Jul-00	024		General Correspondence	FRC 202	Request to re-enroll one of Dr. French's patients J-F		
12-Jul-00	025	V1 P001	General Correspondence	LPT 13295/00	104-Week Carcinogenicity Study of SPM 927 By Oral Administration To Sprague-Dawley Rats (DRAFT PROTOCOL)		
12-Jul-00	025	V1 P030	General Correspondence	1108-005	One-Month Supplemental Range-Finding Toxicity Study of ADD 234037 in Rats		
12-Jul-00	025	V1 P102	General Correspondence	148-235	13-Week Oral Gavage Subchronic Toxicity Study of ADD 234037 in Rats		
12-Jul-00	025	V2 P343	General Correspondence	9817552	Determination of Concentration Levels of ADD 234037 in Rat Plasma: Pharmacokinetic Evaluation Report		
13-Jul-00			FDA Correspondence	FRC 202	FDA fax to approve the re-enrollment of Dr. Fountain's patients requested 6/27/00 SN 022.		
18-Jul-00	026		Information Amendment: Chemistry, Manufacturing an		CMC information regarding capsule formulation		
19-Jul-00	027		Annual Report		Reporting Period: 5/19/99 - 5/18/00		

Monday, November 10, 2008

IND 57,939

Page 16 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
31-Jul-00			FDA Phone Contact	FRC 202	Mr. Foster, SB contacted Ms. Fanari, FDA regarding 7/11/00 SN 024 submission to re-enroll 1 of Dr. French's patients. Ms. Fanari stated the request was being reviewed and she hoped to be in touch in a few days.		
10-Aug-00			FDA Correspondence		FDA faxes CAC recommendations discussion regarding the 2 year carcinogenicity bioassays.		
14-Aug-00			FDA Phone Contact		Mr. Foster, SB contacted Ms. Fanari, FDA to inquire about further comments from the CAC regarding submission dated 7/12/00 SN 025. Ms. Fanari stated none other than the fax dated 8/10/00.		
25-Aug-00			FDA Phone Contact		Mr. Foster, SB contacted Dr. Hershkowitz, FDA regarding need for human in vivo interaction studies given the relative inactivity of a compound in in vitro test systems. Ms. Fanari, FDA returned the call to request the questions be submitted in writing.		
14-Sep-00	028		General Correspondence		Submitted in vitro data from previously submitted nonclinical reports as request from telecon on 8/25/00. Also included proposal for pharmacokinetic interaction studies in healthy volunteers.		
19-Sep-00			FDA Phone Contact	FRC 202	Mr. Foster, SB contacted Ms. Fanari, FDA regarding 9/19/00 SN 029 submission to re-enroll 3 of Dr. Fountain's patients. He apologized for the late notice.		

Monday, November 10, 2008

IND 57,939

Page 17 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>CIOMS Subject No</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
19-Sep-00	029		General Correspondence			Request to re-enroll three of Dr. Fountain's patients CDM, LRE, AWD		
26-Sep-00			FDA Phone Contact		FRC 202	Ms. Fanari, FDA contacted Dr. Blumberg, SB to approve extending 3 of Dr. Fountain's patients (6/27/00 SN 022). Ms. Fanari stated the need to further investigate the NMDA receptor activity; Olney lesion study repeated.		
27-Oct-00			FDA Phone Contact			Mr. Foster, SB contacted Ms. Fanari, FDA to follow-up on submission dated 9/14/00 SN 028. Ms. Fanari stated Biopharmaceutics reviewer would have comments back week Oct 30, comments to SB week Nov 6.		
15-Nov-00			FDA Correspondence			FDA fax containing comments and recommendations in regards to 9/14/00 SN 028 submission.		
21-Nov-00	030		Response to FDA Request for Information			Request to re-enroll two of Dr. Fountain's patients CDM, LRE. Also provided a status update on the report for mice NMDA-induced tox study and the repeat Olney Lesion study.		
07-Dec-00			FDA Phone Contact			Ms. Fanari, FDA contacted Mr. Foster, SB in response to request to re-enroll Dr. Fountain's patients dated 11/21/00 SN 030. Response available week Dec 11.		
07-Dec-00	031		Information Amendment: Clinical			Investigator's Brochure		

Monday, November 10, 2008

IND 57,939

Page 18 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
12-Dec-00			FDA Phone Contact		Ms. Fanari, FDA contacted Dr. Blumberg, SB regarding email dated 12/12/00. Request to re-enroll Dr. Fountain's patients approved (11/21/00 SN 030). Ms. Fanari also provided clarification of "convincing evidence" of efficacy.		
12-Dec-00			FDA Correspondence		Email from Dr. Blumberg, SB to Ms. Fanari, FDA requesting clarification on "convincing evidence" of efficacy. Telecon requested prior to end of December		
13-Dec-00	032		Initial Safety Report	SP588	Mfr. Report No. 000#5#2000-00026 Subject No. 10215/8061 experienced hepatitis.	2000-00026	10215/8061
21-Dec-00			FDA Correspondence	FRC 202	FDA fax to approve the re-enrollment of Dr. Fountain's patients requested 11/21/00 SN 030		
01-Feb-01	033	V1 P1	Information Amendment: Clinical	FRC 101	Double blind, randomized, Placebo controlled, parallel group, single intravenous ascending dose study to determine the tolerability and pharmacokinetic profile of ADD 234037		
01-Feb-01	033	V3 P1	Information Amendment: Clinical	FRC 102	Double blind, randomized, Placebo controlled, parallel group, single oral ascending dose study to determine the tolerability and pharmacokinetic profile of ADD 234037		
01-Feb-01	033	V5 P1	Information Amendment: Clinical	FRC 103	Double blind, randomized, Placebo controlled, parallel group, 7-day oral ascending dose study to determine the tolerability and pharmacokinetic profile of ADD 234037		

Monday, November 10, 2008

IND 57,939

Page 19 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
01-Feb-01	033	V7 P1	Information Amendment: Clinical	FRC 01-201	A Phase II, multicenter, ascending dose assessment study of the safety, tolerability, compatibility, efficacy and pharmacokinetics of harkoseride (ADD 234037) as Adjunctive Therapy in patients with partial Seizures		
06-Feb-01	034		General Correspondence		Request to re-enroll two of Dr. Fountain's patients CDM, LRE.		
06-Feb-01	034		General Correspondence	D00.161/3	Effects of SPM 927 on convulsions induced by NMDA (i.c.v.) in the mouse		
28-Feb-01	035	V1 P1	General Correspondence	LPT 13123/00	13-week subchronic toxicity study of SPM 927 by oral administration to CD-1 mice (DRAFT)		
28-Feb-01	035	V2 P1	General Correspondence	TK 13123	Toxicokinetic evaluation of the study '13-week subchronic toxicity study of SPM 927 by oral administration to CD 1-mice' (DRAFT)		
28-Feb-01	035	V2 P101	General Correspondence	LPT 13124/00	104-week carcinogenicity study of SPM 927 by oral administration to CD-1 mice (DRAFT PROTOCOL)		
28-Feb-01	035	V2 P12	General Correspondence	SSPSS 0735-SP1	Quantitative determination of SPM 927 in mouse plasma specimens from Laboratory of Pharmacology and Toxicology KG Protocol No LPT 13123/00 for Schwarz Pharma AG		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>FDA Phone Contact</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
02-Mar-01				FDA Phone Contact	FRC 202	Mr. Foster, SB contacted Ms. Fanari, FDA to follow-up on request dated 2/6/01 SN 034 to re-enroll Dr. Fountain's patients. Ms. Fanari said the request was approved. Mr. Foster requested the notification in writing.		
06-Mar-01	036	V1 P1		Information Amendment: Pharmacology/Toxicology	PhTox 2259	Harkoseride in preclinical animal models of pain		
06-Mar-01	036	V1 P254		Information Amendment: Pharmacology/Toxicology	LPT 13226/00	2-week Dose-Range-Finding Study for a 9-month Chronic Toxicity Study of SPM 927 by Oral Administration to Beagle Dogs		
06-Mar-01	036	V1 P33		Information Amendment: Pharmacology/Toxicology	LPT 13121/00	Acute Toxicity Study of SPM 927 by Oral Administration to CD-1 mice		
06-Mar-01	036	V1 P81		Information Amendment: Pharmacology/Toxicology	LPT 13122/00	14-day dose-range-finding study for a 13-week subchronic toxicity study of SPM 927 by oral administration to CD-1 mice		
06-Mar-01	036	V2 P1		Information Amendment: Pharmacology/Toxicology	LPT 13227/00	6-month chronic toxicity study of SPM 927 by oral administration to Sprague-Dawley rats		
06-Mar-01	036	V3 P1		Information Amendment: Pharmacology/Toxicology	LPT 13196/00	12-month chronic toxicity study of SPM 927 by oral administration to beagle dogs (INTERIM REPORT)		
06-Mar-01	036	V4 P1		Information Amendment: Pharmacology/Toxicology	1108-003P	Oral (gavage) dosage-range developmental toxicity study of harkoseride in female rats		
06-Mar-01	036	V4 P120		Information Amendment: Pharmacology/Toxicology	1108-003	Combined oral (gavage) fertility and developmental toxicity study of harkoseride (ADD 234037) in rats		

Monday, November 10, 2008

IND 57,939

Page 21 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
06-Mar-01	036	V5 P1	Information Amendment: Pharmacology/Toxicology	1108-004	Oral (gavage) developmental and perinatal/postnatal reproduction toxicity study of harkoseride (ADD 234037) in rats, including a postnatal behavioral/functional evaluation		
06-Mar-01	036	V6 P1	Information Amendment: Pharmacology/Toxicology	1108-002P	Oral (stomach tube) dosage-range developmental toxicity study of harkoseride in female rabbits		
06-Mar-01	036	V6 P145	Information Amendment: Pharmacology/Toxicology	1108-002	Oral (stomach tube) developmental toxicity study of harkoseride in female rabbits		
06-Mar-01	036	V7 P1	Information Amendment: Pharmacology/Toxicology	IPL-R000603	Mutagenicity test on bacteria (Salmonella typhimurium his and Escherichia coli trp) using B.N. Ames's technique with SPM 927		
06-Mar-01	036	V7 P153	Information Amendment: Pharmacology/Toxicology	LPT 13418/00	Exposure of the mouse to SPM 927 after single intraperitoneal administration		
06-Mar-01	036	V7 P42	Information Amendment: Pharmacology/Toxicology	IPL-R000801	Measurement of unscheduled DNA synthesis (UDS) in rat hepatocytes using an In vivo procedure with SPM 927		
07-Mar-01	037		Response to FDA Request for Information		Olney Lesion study - Evaluation of the potential of SPM 927 to induce acute neurotoxic changes in the adult rat brain		
15-Mar-01			FDA Correspondence	FRC 202	FDA fax approving the request of 2/6/01 SN 034 to re-enroll 2 of Dr. Fountain's patients.		
21-Mar-01	038		Initial Safety Report	SP611	Mfr. Report No. 003#5#2001-00021 Subject No. 1008 experienced increased serum potassium	2001-00021	1008

Monday, November 10, 2008

IND 57,939

Page 22 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
22-Mar-01	039		Information Amendment: Clinical		Investigator's Brochure		
23-Mar-01	040		Information Amendment: Chemistry, Manufacturing an		Update to drug substance and drug product to incorporate use of 50 and 100 mg film-coated tablets		
23-Mar-01	041		Protocol Amendment: New Investigator	SP607			
23-Mar-01	041		Information Amendment: Chemistry, Manufacturing an	SP607	Sample clinical supply labels		
23-Mar-01	041		Protocol Amendment: New Protocol	SP607	Original protocol		
04-Apr-01	042		Follow-up Safety Report	SP588	Mfr. Report No. 000#5#2000-00026 Subject No. 10215/8061 experienced hepatitis.	2000-00026	10215/8061
06-Apr-01	043		Follow-up Safety Report	SP611	Mfr. Report No. 003#5#2001-00021 Subject No. 1008 experienced hyperkalemia	2001-00021	1008
20-Apr-01			FDA Phone Contact		Mr. Foster, SB contacted Ms. Fanari, FDA to follow up on review of submission dated 2/28/01 SN035. CAC would review data on 4/23/01. Fax to be received by SB 7-10 days after mtg.		

Monday, November 10, 2008

IND 57,939

Page 23 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
02-May-01			FDA Phone Contact	SP607	Mr. Foster, SB contacted Ms. Fanari, FDA regarding LFT inclusion criteria and ECG reporting recommendations from DACCADP. Dr. Hershowitz will review info from DACCADP 5/8. Mr. Foster requested timeline for feedback as protocol was to be initiated soon.		
03-May-01			FDA Correspondence	LPT 13123/00	FDA fax from CAC regarding 2/28/01 SN 035 submission. Cmte. felt MTD had not been exceeded in the 13-wk study. It was recommended that FDA be notified if excessive mortality is observed in the 2-yr study.		
03-May-01	044		General Correspondence	FRC 202	Request to re-enroll two of Dr. Fountain's patients CDM, LRE.		
03-May-01	044		Response to FDA Request for Information	FRC 202	Response to FDA fax 3/15/01 to provide additional information on patient 02-001 and information on other patients who developed similar etiology.		
15-May-01			FDA Phone Contact	SP607	Mr. Foster, SB contacted Ms. Fanari, FDA regarding Dr. Hershowitz' response to comments from DACCADP. The review was taking longer than anticipated but Ms. Fanari stated SB may submit protocol with understanding that revisions may be required.		
17-May-01	045		Protocol Amendment: Change in Protocol	SP607	Protocol Amendment 1. Incorporates recommendations from DACCADP on LFT entry criteria and additional ECG reporting.		

Monday, November 10, 2008

IND 57,939

Page 24 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
04-Jun-01			FDA Phone Contact		Mr. Foster, SB contacted Ms. Fanari, FDA to follow up on submission dated 3/5/01 SN044 to re-enroll Dr. Fountain's patients. Permission was granted via phone.		
27-Jun-01	046		Protocol Amendment: New Protocol	SP615	Original protocol		
27-Jun-01	046		Protocol Amendment: Change in Protocol	SP615	Protocol Amendment 1. Incorporates recommendations from DACCADP on LFT entry criteria and additional ECG reporting.		
27-Jun-01	046		Information Amendment: CMC Data	SP615	Sample clinical supply labels		
03-Jul-01	047		Protocol Amendment: New Investigator	SP607			
06-Jul-01	048	V1 P1	Information Amendment: Pharmacology/Toxicology	CEREP 817003	Study of compound SPM 927 in various receptor binding and functional monoamine uptake assays		
06-Jul-01	048	V1 P139	Information Amendment: Pharmacology/Toxicology	CERB 20000378F	SPM 927: Evaluation of effect on respiration in the unrestrained conscious rat following single oral administration		
06-Jul-01	048	V1 P265	Information Amendment: Pharmacology/Toxicology	CERB 20000380F	SPM 927: Evaluation of effect on intestinal transit in the rat following single oral administration		
06-Jul-01	048	V1 P40	Information Amendment: Pharmacology/Toxicology	CEREP 817004	Study of seven compounds in various receptor binding assays		

Monday, November 10, 2008

IND 57,939

Page 25 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
			<i>Type</i>	<i>Amendment</i>			<i>Mfr Control No</i>	<i>Subject No</i>	
06-Jul-01	048	V1 P56	Information Amendment: Pharmacology/Toxicology	SPM 927: Evaluation of effect on cardiac action potential in isolated canine Purkinje fibres	DERB 20000377f				
06-Jul-01	048	V2 P1	Information Amendment: Pharmacology/Toxicology	Acute skin irritation test (patch test) of SPM 927 in rabbits	LPT 13356/00				
06-Jul-01	048	V2 P27	Information Amendment: Pharmacology/Toxicology	Acute eye irritation study of SPM 927 by instillation into the conjunctival sac of rabbits	LPT 13760/00				
06-Jul-01	048	V2 P55	Information Amendment: Pharmacology/Toxicology	Examination of SPM 927 in the skin sensitisation test in guinea-pigs according to Magnusson and Kligman	LPT 13355/00				
06-Jul-01	048	V2 P91	Information Amendment: Pharmacology/Toxicology	(14C)-SPM 927: Quantitative whole-body autoradiography following oral and intravenous administration to the pigmented rat	699/17-D1140				
06-Jul-01	049		Initial Safety Report	Mfr. Report No. 003#5#2001-00018(5) Subject No. 1003 had severe abdominal pain possibly related to study drug. Probable that event was related to underlying concomitant disease. Further diagnostic testing required.	SP611		2001-00018(5)		1003
18-Jul-01	050		Annual Report	Period covering May 19, 2000 through April 18, 2001					
19-Jul-01			FDA Phone Contact	Dr. Broadbent, FDA contacted Alan Blumberg, SB regarding additional stability data to support protocol SP615.	SP615				
20-Jul-01			Response to FDA Request for Information	Email response to FDA contact from Dr. Broadbent for additional stability data.	SP615				

Monday, November 10, 2008

IND 57,939

Page 26 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Type</i>	<i>Location</i>			<i>Mfr Control No</i>	<i>Subject No</i>
23-Jul-01	051	Response to FDA Request for Information		SP615	Response to FDA contact from Dr. Broadbent for additional stability data.		
26-Jul-01		FDA Phone Contact		stability SN051	Dr. Broadbent, FDA contacted Eric Foster regarding stability be submitted as amendment to IND, Eric referred him to SN 051		
26-Jul-01		FDA Phone Contact		SP615	Eric Foster contacted Fanari, FDA to discuss protocol SP615 ext. and finds it acceptable for patients in FRC202 and SP607 to enroll in SP615		
01-Aug-01	052	Protocol Amendment: New Investigator		SP607			
06-Aug-01	053	Initial Safety Report		SP647		2001-00065(0)	1019
06-Aug-01	053	Initial Safety Report		SP620		2001-00067(0)	17917/8008
30-Aug-01	054	Follow-up Safety Report		SP620		2001-00067	17917/8008
07-Sep-01	055	Protocol Amendment: New Investigator		FRC01-202			
07-Sep-01	055	Protocol Amendment: New Investigator		SP615			
07-Sep-01	055	Protocol Amendment: New Investigator		SP607			
25-Sep-01	056	Initial Safety Report		SP647		2001-00074	1010

Monday, November 10, 2008

IND 57,939

Page 27 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>				<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
09-Oct-01			FDA Phone Contact			New IND required for IV formulation of SPM 927		
24-Oct-01	057		Protocol Amendment: Change in Protocol		SP615	Amendment 2		
29-Oct-01	058	V1 P1	Information Amendment: Pharmacology/Toxicology		G0011Sch291E	Examination of the effects of SPM 927, SPM G, and SPM I on KCNQ2/KCNQ3-mediated potassium currents		
29-Oct-01	058	V1 P22	Information Amendment: Pharmacology/Toxicology		6958-103	Neuronal vacuolization study with SPM 927 in rats		
29-Oct-01	058	V2 P1	Information Amendment: Pharmacology/Toxicology		DERB 20000379F	Behavioural Irwin test and effect on body temperature following single oral administration in the rat		
29-Oct-01	058	V2 P109	Information Amendment: Pharmacology/Toxicology		DERB 20000381F	Evaluation of interactions with neurotransmitters (acetylcholine, histamine, serotonin) and barium chloride on isolated ileum of guinea-pigs		
29-Oct-01	058	V3 P1	Information Amendment: Pharmacology/Toxicology		DERB 20000376F	Evaluation of haemodynamic effects and electrocardiogram following intravenous dosing in the anesthetised dog		
29-Oct-01	058	V4 P1	Information Amendment: Pharmacology/Toxicology		LPT 13123/00	13-week subchronic toxicity study of SPM 927 by oral administration to CD-1 mice		
29-Oct-01	058	V6 P1	Information Amendment: Pharmacology/Toxicology		LPT 13227/00	6-month chronic toxicity study of SPM 927 by oral administration to sprague-Dawley rats		
13-Nov-01	059		Protocol Amendment: New Investigator		SP607			

Monday, November 10, 2008

IND 57,939

Page 28 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>CIOMS Subject No</i>			<i>Mfr Control No</i>	<i>Subject No</i>
13-Nov-01	059		Protocol Amendment: New Investigator		SP615			
27-Nov-01	060		Protocol Amendment: New Investigator		SP667			
27-Nov-01	060		Information Amendment: CMC Data		SP667	Sample clinical supply labels		
27-Nov-01	060		Protocol Amendment: New Protocol		SP667			
04-Dec-01	061		Information Amendment: Pharmacology/Toxicology		LPT 13196/00	12-month chronic toxicity study of SPM 927 by oral administration to beagle dogs		
13-Dec-01	062		Information Amendment: Clinical			Investigator's Brochure Addendum		
20-Dec-01	063		Information Amendment: CMC Data			Revisions to the DS synthesis, specs and methods, alternate DS supplier, and update in stability.		
21-Dec-01	064		Initial Safety Report		SP607		2001-00081	1562
17-Jan-02	065		Protocol Amendment: Change in Protocol		SP615	Amendment 3		
17-Jan-02	065		Protocol Amendment: New Investigator		SP607	New and Revised		
31-Jan-02	066		Follow-up Safety Report		SP620		2001-00067	17917/8008
14-Feb-02	067		Protocol Amendment: New Investigator		SP607	Revised 1572		

Monday, November 10, 2008

IND 57,939

Page 29 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
14-Feb-02	067		Protocol Amendment: New Investigator	SP667	New Investigators		
14-Mar-02	068		Protocol Amendment: New Investigator	SP607	Revised Investigator		
14-Mar-02	068		Protocol Amendment: New Investigator	SP667	New Investigators		
21-Mar-02	069		Information Amendment: CMC Data	SP667	Sample clinical supply label for transition phase		
21-Mar-02	069		Protocol Amendment: Change in Protocol	SP667	Amendment 1		
08-Apr-02	070		Protocol Amendment: New Investigator	SP607	New and revised investigators		
08-Apr-02	070		Protocol Amendment: New Investigator	SP615	New and revised investigators		
08-Apr-02	070		Protocol Amendment: New Investigator	SP667	New investigators		
09-Apr-02	071		Information Amendment: Clinical	SP620	Double-blind, placebo-controlled, parallel group trial to evaluate the pharmacokinetics and tolerability of SPM 927 (harkoseride) following single and multiple oral administration to 48 healthy Caucasian subjects differing in age and gender		
09-Apr-02	072		Follow-up Safety Report	SP607		2001-00081	1562

Monday, November 10, 2008

IND 57,939

Page 30 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>Sub</i>			<i>Mfr Control No</i>	<i>Subject No</i>
16-Apr-02	073		Protocol Amendment: New Investigator		SP615	New investigator		
16-Apr-02	073		Protocol Amendment: New Investigator		SP667	New investigators		
19-Apr-02	074		Initial Safety Report		SP615		2002-00044	10027
30-Apr-02	075		Follow-up Safety Report		SP615		2002-00044	10027
14-May-02	076		Protocol Amendment: New Investigator		SP667	New and revised investigators		
04-Jun-02	077		General Correspondence			Send FDA interim report after 39 weeks from the 104-week rat carcinogenicity study for CAC review.		
18-Jun-02	078		Follow-up Safety Report		SP607		2001-00081	1562
20-Jun-02	079		Protocol Amendment: New Investigator		SP615	Revised investigator		
20-Jun-02	079		Protocol Amendment: New Investigator		SP667	New investigators		
21-Jun-02			FDA Phone Contact			Ms. Fanari, FDA, calls with review status of carcinogenicity study for CAC review, CAC has not yet scheduled a meeting but thinks it will be 2nd week July		
21-Jun-02	080	v1 p1	Information Amendment: Pharmacology/Toxicology		CEREP 817005	Assessment of analgesic effects of SPM-G (gabapentin), SPM 927 and SPM-I in carrageenan-induced hyperalgesia in rats and in formalin test in mice		

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
21-Jun-02	080	v1 p106	Information Amendment: Pharmacology/Toxicology	LPT 14537/1/01	Local tolerance test of SPM 927 in rabbits after a single intravenous, intraarterial, paravenous, subcutaneous and intramuscular administration		
21-Jun-02	080	v1 p146	Information Amendment: Pharmacology/Toxicology	Covance 699/15	14C-SPM 927: Placental transfer, lacteal secretion and transfer to suckling neonates in the rat		
21-Jun-02	080	v1 p22	Information Amendment: Pharmacology/Toxicology	CEREP 5498	In-vitro pharmacology - study of SPM 927		
21-Jun-02	080	v1 p231	Information Amendment: Pharmacology/Toxicology	Covance 699/01E	14C-SPM 927 In vitro binding to plasma proteins in mouse, rat, dog and human		
21-Jun-02	080	v1 p43	Information Amendment: Pharmacology/Toxicology	Sams-Dodd S.L.	Electrophysiological characterization of SPM 927		
21-Jun-02	080	v1 p57	Information Amendment: Pharmacology/Toxicology	Partners Pharm.	SPM 927-effects on the corneal reflex in the conscious rabbit		
21-Jun-02	080	v1 p82	Information Amendment: Pharmacology/Toxicology	LPT 14536/01	Examination of SPM 927 for compatibility and hemolytic properties in citrate-anticoagulated human blood (in-vitro)		
21-Jun-02	081		7-Day Safety Report Fax	SP655	Fax FDA 7-day report of Mfr. Report No. 000#5#2002-00095 Subj. 10001/80037	2002-00095	10001/80037
15-Jul-02			FDA Correspondence		FDA faxes CAC agreement with our request to increase the high dose for fernal rats from 160 to 180 mg/kg/day in 9-jul-2002 meeting.		
17-Jul-02	082		Protocol Amendment: New Investigator	SP607	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 32 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Type</i>	<i>Location</i>			<i>Mfr Control No</i>	<i>Subject No</i>
17-Jul-02	082	Protocol Amendment: New Investigator		SP667	New and revised investigators		
22-Jul-02	083	Annual Report			Period covering 19-apr-01 through 18-apr-02		
30-Jul-02	084	Information Amendment: CMC Data			Scale-up of DS synthesis by SIFA and increase in batch size of 50 and 100mg film coated tablets.		
02-Aug-02	085	7-Day Safety Report		SP655		2002-00136	10266/80011
08-Aug-02		FDA Phone Contact		SP655	Call to Melina Fanari, FDA, advance notification of 7 Day Reportable AE. Mfr. Report No. 000#5#2002-00155 Subj. No. 10097/80025		
09-Aug-02		Other			Email Ms. Fanari, FDA, initial CIOMS report for Mfr. Report No. 000#5#2002-00155, follow-up report will be sent early next week.		
12-Aug-02	086	7-Day Safety Report		SP655		2002-00155	10097/80025
21-Aug-02	087	Initial Safety Report		SP615		2002-00143	10378/10378
23-Aug-02	088	Protocol Amendment: New Investigator		SP667	New and Revised Investigators		
23-Aug-02	088	Protocol Amendment: New Investigator		SP607	Revised Investigators		
28-Aug-02	089	Follow-up Safety Report		SP655		2002-00155	10097/80025

Monday, November 10, 2008

IND 57,939

Page 33 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
03-Sep-02			FDA Correspondence	SP655	Serial No. 089 should have been entitled: 'Follow-up Report', not 'Initial Safety Report'.		
05-Sep-02	090		Initial Safety Report	SP667		2002-00133	17307/80033
16-Sep-02	091		Follow-up Safety Report	SP655		2002-00095	10001/80037
16-Sep-02	091		Follow-up Safety Report	SP655		2002-00155	10097/80025
16-Sep-02	092		Initial Safety Report	SP667		2002-00153	17401/80030
19-Sep-02	093		Follow-up Safety Report	SP615		2002-00044	10027
27-Sep-02			7-Day Safety Report	SP643	Email Melinda Fanari, FDA, notification of 7-day safety report is coming		
27-Sep-02			Other		Ms. Griffis, FDA, emails new name and address.		
27-Sep-02	094		7-Day Safety Report	SP643		2002-00223	10020/80011
27-Sep-02	095		Protocol Amendment: New Investigator	SP615	New Investigator		
27-Sep-02	095		Protocol Amendment: New Investigator	SP667	New Investigators		
30-Sep-02	096		General Correspondence	SP615	Terminate Investigator Dr. D. Frank Fleming as investigator to SP615		

Monday, November 10, 2008

IND 57,939

Page 34 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
30-Sep-02	096		General Correspondence	SP667	Terminate Investigator Dr. D. Frank Fleming as investigator for SP667		
30-Sep-02	097		Follow-up Safety Report	SP667		2002-00153	17401/80030
01-Oct-02	098		Initial Safety Report	SP655		2002-00212	10223/80104
02-Oct-02			Other		Email Ms. Griffiths, FDA, CIOMS report for Mfr. Report No. 000#5#2002-00212 due to courier loss of package.		
04-Oct-02			General Correspondence	SP667	Fax 7-day safety report for Mfr. Report No. 000#5#2002-00244 Subj. No. 12803/80017		
04-Oct-02	099		Initial Safety Report	SP667		2002-00244	12803/80017
23-Oct-02	100		Protocol Amendment: New Investigator	SP667	New investigators		
23-Oct-02	100		Protocol Amendment: New Investigator	SP615	New investigators		
23-Oct-02	100		Protocol Amendment: New Investigator	SP607	Revised investigators		
23-Oct-02	101		Follow-up Safety Report	SP667		2002-00133	17307/80033
23-Oct-02	101		Follow-up Safety Report	SP667		2002-00244	12803/80017
06-Nov-02	102		Follow-up Safety Report	SP643		2002-00223	10020/80011

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
			<i>Type</i>	<i>Sub</i>			<i>Mfr Control No</i>	<i>Control No</i>	
14-Nov-02	103		Initial Safety Report		SP665		2002-00296		10234
18-Nov-02	104		Initial Safety Report		SP614		2002-00298		1520/8265
21-Nov-02	105		Protocol Amendment: New Investigator		SP667	New investigators			
21-Nov-02	105		Protocol Amendment: New Investigator		SP615	New investigators			
25-Nov-02	106		General Correspondence			Submit 67 week interim report and proposal to increase dose in female rats from 180 to 200 mg/kg/day.			
25-Nov-02	106		General Correspondence		LPT 13295/00	104-week carcinogenicity study of SPM 927 by oral administration to sprague-dawley rats (INTERIM REPORT)			
26-Nov-02	107		Follow-up Safety Report		SP614		2002-00296		2002-00296
26-Nov-02	107		Response to FDA Request for Information			Submit follow-up safety information in response to FDA request			
26-Nov-02	107		Follow-up Safety Report		SP665		2002-00298		2002-00298
26-Nov-02	108		Initial Safety Report		SP665		2002-00306		10141/10141
09-Dec-02	109		Initial Safety Report		SP667		2002-00287		10202/80077
12-Dec-02	110		Follow-up Safety Report		SP665		2002-00306		10141/10141

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
16-Dec-02			FDA Phone Contact		Call Ms. Ware, FDA, to check on CAC meeting date to discuss our request to increase dose in female rat from 180 to 200 mg/kg/day submitted 25-nov-2002.		
19-Dec-02	111		Protocol Amendment: New Investigator	SP667	Revised Investigator		
19-Dec-02	111		Protocol Amendment: New Investigator	SP615	New Investigators		
20-Dec-02			Initial Safety Report	SP667	Email Ms. Ware 7-day safety report Mfr. Report No. 000#5#2002-00352	2002-00352	
20-Dec-02			FDA Phone Contact		Ms. Ware, FDA, calls to state pharmacology reviewer okays dose adjustment in the rat 2 year carcinogenicity study further executive CAC comment is not required.		
20-Dec-02	112		Initial Safety Report	SP667		2002-00352	17204/80105
02-Jan-03			7-Day Safety Report	SP614	Email Ms. Ware 7-day safety report Mfr. Report No. 000#5#2002-00364	2002-00364	1047/8005
02-Jan-03			7-Day Safety Report	SP614	Email Ms. Ware 7-day safety report Mfr. Report No. 000#5#2002-00364	2002-00364	
02-Jan-03	114		Follow-up Safety Report	SP665		2002-00306	10141/10141
22-Jan-03	115		Protocol Amendment: New Investigator	SP615	New and revised investigators		
07-Feb-03	116		Follow-up Safety Report	SP614		2002-00364	1047/8005

Monday, November 10, 2008

IND 57,939

Page 37 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
07-Feb-03	116		Follow-up Safety Report	SP615		2002-00143	10378/10378
07-Feb-03	116		Follow-up Safety Report	SP667		2002-00287	10202/80077
07-Feb-03	116		Follow-up Safety Report	SP667		2002-00352	17204/80105
20-Feb-03	0117		Protocol Amendment: New Investigator	SP615	New and revised investigators		
24-Feb-03	0118		Initial Safety Report	SP667		2003-00048	15006/80139
10-Mar-03	0119		Initial Safety Report	SP667		2003-00060	12304/80097
17-Mar-03	0120		Follow-up Safety Report	SP667		2002-00352	17204/80105
17-Mar-03	0121		Follow-up Safety Report	SP655		2002-00095	10001/80037
17-Mar-03	0121		Response to FDA Request for Information	SP655	Respond to FDA request 20-feb-03 with follow-up safety report regarding encephalopathy case.		
20-Mar-03	0122		Protocol Amendment: New Investigator	SP667	New and revised investigators		
20-Mar-03	0122		Protocol Amendment: New Investigator	SP615	New investigator		
28-Mar-03	0123		General Correspondence		Submit response to IND 62,244 safety and pharm/tox information to neuropharm division		

Monday, November 10, 2008

IND 57,939

Page 38 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>Amendment</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
28-Mar-03	0123			Information Amendment: Pharmacology/Toxicology		Submit response to IND 62,244 safety and pharm/tox information to neuropharm division		
28-Mar-03	0123	v1 p189		Information Amendment: Pharmacology/Toxicology	020316.TDA	Effect of SPM 927 on cloned hERG channels expressed in mammalian cells		
28-Mar-03	0123	v1 p210		Information Amendment: Pharmacology/Toxicology	E-01-014-001	Electrophysiological examination of activity of SPM 927 on the SCN5A-sodium channel expressed in CHO cells		
28-Mar-03	0123	v1 p240		Information Amendment: Pharmacology/Toxicology	011119.TDA	Effect of SPM 927 on the human cardiac I _{Na} (hHNA) current expressed in mammalian cells		
28-Mar-03	0123	v1 p276		Information Amendment: Pharmacology/Toxicology	SB01D01	SPM 927: in vitro effect on I _{Na} and I _{Ca} recorded from human atrial myocytes		
28-Mar-03	0123	v1 p303		Information Amendment: Pharmacology/Toxicology	LPT 15066/01	Examination of SPM 927 on L-type Ca ²⁺ inward current in isolated ventricular myocytes of the guinea pig		
28-Mar-03	0123	v1 p347		Information Amendment: Pharmacology/Toxicology	0247XH15.004	Cardiovascular evaluation of DD 234037 in Non-human primates		
28-Mar-03	0123	v1 p90		Information Amendment: Pharmacology/Toxicology	20000377P	Evaluation of effect on cardiac action potential in isolated canine purkinje fibres		
28-Mar-03	0123	v2 p1		Information Amendment: Pharmacology/Toxicology	20000376P	Evaluation of haemodynamic effects and electrocardiogram following intravenous dosing in the anesthetised dog		
31-Mar-03	0124		Meeting Request			Request Type B meeting with FDA to discuss proposed phase 3 development.		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
11-Apr-03	0125		Follow-up Safety Report	SP643		2002-00223	10020/80011
14-Apr-03			FDA Phone Contact		Dr. Fenney, FDA, call to deny meeting request due to not enough clinical data to discuss at this time.		
21-Apr-03	0126		Protocol Amendment: New Investigator	SP667	New investigators		
21-Apr-03	0126		Protocol Amendment: New Investigator	SP615	New and revised investigators		
28-Apr-03			FDA Phone Contact		Ms. Griffith, FDA, calls to discuss denial of meeting request. Suggest future request include all completed study descriptions and all disciplines. Any phase 3 protocol should be submitted for complete review and comment by FDA before proceeding.		
30-Apr-03	0127		Follow-up Safety Report	SP667		2002-00352	17204/80105
05-May-03	0128		Protocol Amendment: Change in Protocol	SP667	Amendment 2		
09-May-03	0129		Initial Safety Report	SP667		2003-00137	15009/80150
16-May-03			FDA Phone Contact		Call Ms. Griffis, FDA, to see if a separate IND is required for an intravenous formulation of SPM 927; should cross reference the tablet IND and submit IV specific information.		
21-May-03	0130		Protocol Amendment: New Investigator	SP615	New investigators		

Monday, November 10, 2008

IND 57,939

Page 40 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
21-May-03	0130		Protocol Amendment: New Investigator	SP667	New and revised investigators		
22-May-03	0131		Follow-up Safety Report	SP667		2003-00060	12304/80097
28-May-03	0132		General Correspondence		Fax Request for comment to FDA regarding 104-week carcinogenicity study increased mortality.		
28-May-03	0132		Request FDA Comment		Schwarz requests CAC review and comment to request to terminate 104-week mouse carcinogenicity study if mortality reaches 60% due to mortality increasing excessively.		
30-May-03			FDA Correspondence		Ms. Griffiths, FDA, emails response to our request to terminate the 104-week carcinogenicity study due to excessive deaths. FDA states we should not stop the study.		
10-Jun-03	0133	v1 p1	Information Amendment: Pharmacology/Toxicology	CEREP 6065	In vitro pharmacology		
10-Jun-03	0133	v1 p122	Information Amendment: Pharmacology/Toxicology	D00.271/2/A	SPM 927 effects in tests for general behavior, motor incoordination and antinociception in the mouse and the rat (i.p. and p.o. administration)		
10-Jun-03	0133	v1 p21	Information Amendment: Pharmacology/Toxicology	106-02-01	Effects of SPM 927 on voltage-activated TTX-sensitive and TTX-insensitive sodium currents		
10-Jun-03	0133	v1 p29	Information Amendment: Pharmacology/Toxicology	D02.274/2	SPM 927, SPM 6953 and SPM 12809 evaluation for anticonvulsant activity in the mouse (i.p. administration)		

Monday, November 10, 2008

IND 57,939

Page 41 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>Amendment</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
10-Jun-03	0133	v1 p340		Information Amendment: Pharmacology/Toxicology	D01.171/2	Effects of SPM 927 in comparison with carbamazepine, levitiracetam, gabapentin and pregabalin on neuropathic pain (chung model) in the rat (i.p. administration)		
10-Jun-03	0133	v1 p403		Information Amendment: Pharmacology/Toxicology	Krause and Stohr	SPM 927 effects on mechanical hyperalgesia in the rat model of freund's complete adjuvans induced arthritis (i.p. administration)		
10-Jun-03	0133	v1 p423		Information Amendment: Pharmacology/Toxicology	PML 2002-C167	Anti-epileptic action of SPM 927 in the WAG/Rij rat, a model for absence epilepsy		
10-Jun-03	0133	v1 p454		Information Amendment: Pharmacology/Toxicology	Sams-Dodd, SL	Electrophysiological characterization of SPM 927		
10-Jun-03	0133	v1 p67		Information Amendment: Pharmacology/Toxicology	D01.145/1/B	SPM 927 effects in the two-phase formalin paw test in the mouse and the rat (i.p. administration)		
10-Jun-03	0133	v2 p1		Information Amendment: Pharmacology/Toxicology	MDS 9825451	Determination of concentration levels of ADD 234037 in dog plasma		
10-Jun-03	0133	v2 p156		Information Amendment: Pharmacology/Toxicology	NRPB-M1234	Assessment of the radiation dose received by male human volunteers following the oral and intravenous administration of [14C]-SPM 927		
10-Jun-03	0133	v2 p165		Information Amendment: Pharmacology/Toxicology	ASI 0699-HAADV	Analysis of ADD-234037 in human plasma by LC/MS/MS		
10-Jun-03	0133	v2 p193		Information Amendment: Pharmacology/Toxicology	MDS 9827351	Ultrafiltration using the amicon MPS-1 for assessing ADD 234037 in human plasma protein binding		

Monday, November 10, 2008

IND 57,939

Page 42 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
10-Jun-03	0133	v2 p215	Information Amendment: Pharmacology/Toxicology	Marzin	Expert report on the mutagenicity of SPM 927		
10-Jun-03	0133	v2 p223	Information Amendment: Pharmacology/Toxicology	148/235	13-week oral gavage subchronic toxicity of ADD 234037 in rats		
10-Jun-03	0133	v2 p245	Information Amendment: Pharmacology/Toxicology	LPT 15654/02	Pharmacokinetic study in the male beagle dog after repeated (twice daily) oral administration of SPM 927		
10-Jun-03	0133	v2 p367	Information Amendment: Pharmacology/Toxicology	BA 555-02	Investigation of the cytochrome P450 1A2 and 3A4 induction potential of the compound SPM 927 in cryopreserved human hepatocytes		
10-Jun-03	0133	v2 p385	Information Amendment: Pharmacology/Toxicology	BA 481-03	Interaction of the compounds SPM 927 and SPM 12809 (desmethyl-SPM 927) with the cytochrome P450 isoenzymes 1A2, 3A4, 2C9, 2C19 and 2D6		
10-Jun-03	0133	v2 p427	Information Amendment: Pharmacology/Toxicology	BA 481-03	Amendment 1		
24-Jun-03	0134		Protocol Amendment: New Investigator	SP615	New investigators		
24-Jun-03	0134		Protocol Amendment: New Investigator	SP667	New investigators		
25-Jun-03	0135		Information Amendment: Clinical		Revised Investigator's Brochure dated February 2003		
25-Jun-03	0135		Information Amendment: Clinical		Revised investigator's brochure		

Monday, November 10, 2008

IND 57,939

Page 43 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
26-Jun-03	0136		Request FDA Comment	SP755	A multi., double-blind, randomized, placebo-controlled, parallel-group trial to inv. the efficacy and safety of SPM 927 (200mg and 400mg/day) as adjunctive therapy in subjects with partial seizures with our without secondary generalization draft protoco		
26-Jun-03	0136		General Correspondence		Submit safety information for FDA agreement it is safe to proceed with development of SPM 927 in epilepsy.		
26-Jun-03	0136		Request FDA Comment	SP607	An open label, dose titration trial to determine tolerability and efficacy of oral SPM 927 as adjunctive therapy in patients with partial seizures with or without secondary generalization.		
26-Jun-03	0136		Request FDA Comment	SP754	A multicenter, double-blind, randomized, placebo-controlled, parallel-group trial to investigate the efficacy and safety of SPM 927 (600mg/day) as adjunctive therapy in subjects with partial seizures with our without secondary generalization draft protoco		
27-Jun-03	0137		7-Day Safety Report	SP615		2003-00211	11778
10-Jul-03	0138		Information Amendment: CMC Data		Submit revised CMC data and updated stability information.		
11-Jul-03	0139		General Correspondence	SP665	Notify FDA of subject no. 10353 in protocol SP665 where a prolongation in QT interval was noted in the immediate overread; however, repeat ECGs were not performed in compliance with the protocol amendment.		

Monday, November 10, 2008

IND 57,939

Page 44 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
16-Jul-03	0140		Initial Safety Report	SP667		2002-00202	11801/80028
17-Jul-03	0141		Annual Report		Period covering 19-apr-2002 through 18-apr-2003		
21-Jul-03	0142		Initial Safety Report	SP615		2003-00230	11804/11804
21-Jul-03	0143		Protocol Amendment: New Investigator	SP615	New investigators		
22-Jul-03	0144		Initial Safety Report	SP665		2003-00222	10353/10353
31-Jul-03			7-Day Safety Report Fax	SP615	Fax Melina Griffis, FDA, 7-day safety report for Mfr. Report No. 00#5#2003-00248 Subj. No. 10502	2003-00248	10502
31-Jul-03			7-Day Safety Report Fax	SP615	Fax Melina Griffis, FDA, 7-day safety report for Mfr. Report No. 00#5#2003-00248 Subj. No. 10502	2003-00248	10502
31-Jul-03	0145		7-Day Safety Report	SP615		2003-00248	10502
11-Aug-03	0146		Initial Safety Report	SP615		2003-00262	11777
11-Aug-03	0147		Follow-up Safety Report	SP667		2003-00137	15009/80150
11-Aug-03	0147		Follow-up Safety Report	SP615		2003-00230	11804/11804
18-Aug-03	0148		Initial Safety Report	SP667		2003-00266	15015/80177
18-Aug-03	0149		Follow-up Safety Report	SP615		2003-00211	11778

Monday, November 10, 2008

IND 57,939

Page 45 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
18-Aug-03	0149		Follow-up Safety Report	SP665		2003-00222	10353
21-Aug-03	0150		Protocol Amendment: New Investigator	SP615	New investigators		
21-Aug-03	0150		Protocol Amendment: New Investigator	SP667	New investigator		
26-Aug-03			FDA Phone Contact		Ms. Griffiths, FDA, calls to schedule meeting on 14 or 15 of September to review design of our phase 3 epilepsy studies.		
27-Aug-03	0151		Information Amendment: Clinical		Revised investigator's brochure		
28-Aug-03			FDA Phone Contact		Call Ms. Griffiths, FDA, to notify division that DACCADP for SPM 927 neuropathic pain had QTc prolongation concerns and was reviewing the ECG data submitted on 14-aug-2003.		
28-Aug-03			SB Meeting Minutes		Email Ms. Griffiths, FDA, minutes from end of phase 2 meeting with DACCADP for SPM 927 for neuropathic pain.		
29-Aug-03	0152		General Correspondence		Submit ECG data provided to DACCADP to IND 62,244 to Neuropharm FDA division.		
10-Sep-03	0153		Follow-up Safety Report	SP615		2003-00262	11777
10-Sep-03	0153		Follow-up Safety Report	SP667		2003-00266	15015/80177

Monday, November 10, 2008

IND 57,939

Page 46 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
15-Sep-03			FDA Phone Contact		Dr. Hershkowitz, FDA medical officer, calls to discuss our 26-jun-2003 package requesting assessment if safe to proceed with phase 2b/3 program. Discuss concerns over QTc prolongation, ECG data presented and case of toxic hepatitis.		
16-Sep-03	0154		Initial Safety Report	SP667		2003-00298	11910
16-Sep-03	0155		Follow-up Safety Report	SP615		2003-00211	11778
17-Sep-03			FDA Phone Contact		Ms. Griffiths, FDA, calls to discuss FDA meeting results; no safety concerns but wants cardiac safety study started. Some pk recommendations will be coming in writing to the protocols soon.		
22-Sep-03	0156		Protocol Amendment: New Investigator	SP667	Revised investigator		
22-Sep-03	0156		Protocol Amendment: New Investigator	SP615	New investigator		
22-Sep-03	0157		Initial Safety Report	SP667		2003-00313	13206/10730
24-Sep-03	0158		7-Day Safety Report	SP615		2003-00318	10856
29-Sep-03	0159		Initial Safety Report	SP615		2003-00321	11177
06-Oct-03	0160		Initial Safety Report	SP615		2003-00323	10616/10538
06-Oct-03	0161		Follow-up Safety Report	SP667		2003-00137	15009/80150

Monday, November 10, 2008

IND 57,939

Page 47 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
14-Oct-03			FDA Phone Contact		Ms. Griffis, FDA, returns call to request three desk copies of IV IND, QT protocol does not fall under special protocol assessment, DNDP will defer review of protocol to DACADP, and she is awaiting comments from med reviewer on safety pkg 26-jun-2003.		
15-Oct-03	0162		Follow-up Safety Report	SP615		2003-00321	11177
17-Oct-03	0163		General Correspondence		Submit QTc protocol plan and request teleconference with FDA to discuss comments and plan once FDA review of plan is completed.		
17-Oct-03	0163		Request FDA Comment		QTc protocol plan		
22-Oct-03	0164		Follow-up Safety Report	SP615		2003-00321	11177
23-Oct-03	0165		Protocol Amendment: New Investigator	SP615	New investigators		
23-Oct-03	0166		Initial Safety Report	SP667		2003-00369	15803/80296
24-Oct-03			FDA Phone Contact		Ms. Griffis, FDA, calls with update on status of written response to safety package submitted 26-jun-2003. Has all comments except medical reviewer and hopes to get these week of 27-oct-2003.		
31-Oct-03	0167		7-Day Safety Report	SP665		2003-00376	10253
04-Nov-03	0168		Initial Safety Report	SP665		2003-00373	10241

Monday, November 10, 2008

IND 57,939

Page 48 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
04-Nov-03	0169		Follow-up Safety Report	SP667		2003-00369	15803/80296
06-Nov-03	0170		Initial Safety Report	SP665		2003-00384	10261
07-Nov-03	0171		Protocol Amendment: Change in Protocol	SP667	Amendment 3		
18-Nov-03	0172		Initial Safety Report	SP665		2003-00393	10344
19-Nov-03	0173	v1 p1	Information Amendment: Clinical	SP600	Open-label randomized, single dose, two-way cross-over study to evaluate the effect of food on the bioavailability of SPM 927 (harkoseride) in healthy male caucasian volunteers.		
19-Nov-03	0173	v3 p1	Information Amendment: Clinical	SP601	Open-label randomized, multiple dose, cross-over study to evaluate the pharmacokinetic effect of SPM 927 (harkoseride) on valproic acid (VPA) in 16 healthy male caucasian volunteers.		
20-Nov-03	0174		Protocol Amendment: New Investigator	SP615	New and revised investigators		
20-Nov-03	0174		Protocol Amendment: New Investigator	SP667	Revised investigators		
02-Dec-03	0175		Follow-up Safety Report	SP667		2002-00244	12803/80017
03-Dec-03			FDA Correspondence		FDA comments to safety package submitted 26-jun-2003. Clinical comments will be sent separately.		
03-Dec-03	0176		Follow-up Safety Report	SP655		2002-00095	10001/80037
<i>Monday, November 10, 2008</i>				<i>IND 57,939</i>		<i>Page 49 of 138</i>	

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
			<i>Type</i>				<i>Mfr Control No</i>		
05-Dec-03	0177		Initial Safety Report		SP667		2003-00287		10404/80291
05-Dec-03	0178		Follow-up Safety Report		SP615		2002-00044		10027/10027
17-Dec-03	0179		Response to FDA Request for Information		SP615	Respond with follow-up safety information requested in a telephone call from Norman Herschkowitz, FDA, received 16-dec-2003.	2003-00248		10502
17-Dec-03	0179		Follow-up Safety Report		SP615		2003-00248		10502
18-Dec-03	0180		Protocol Amendment: New Investigator		SP615	New investigator			
18-Dec-03	0181		Protocol Amendment: Change in Protocol		SP615	Protocol amendment 4			
19-Dec-03	0182		Initial Safety Report		SP615		2003-00450		11488
23-Dec-03	0183		Follow-up Safety Report		SP667		2003-00287		10404/80291
30-Dec-03	0184		Initial Safety Report		SP615		2003-00474		11503
09-Jan-04	0185		Protocol Amendment: New Protocol		SP754	New Protocol			
09-Jan-04	0185		Protocol Amendment: New Investigator		SP754	New Investigator			
20-Jan-04	0186		Protocol Amendment: New Investigator		SP615	New and revised investigators			

Monday, November 10, 2008

IND 57,939

Page 50 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Type</i>	<i>Location</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Jan-04	0186	Protocol Amendment: New Investigator		SP667	Revised investigators		
21-Jan-04	0187	General Correspondence		SP615	Provide revised FDA form 1572s inadvertently left out of new investigator submission 20-Jan-2004 serial no. 0186.		
06-Feb-04		FDA Phone Contact			Call Ms. Griffis, FDA, to confirm that separate NDAs are required of each type of dosage form. Additionally if time allows both could be discussed at the same EOP2 meeting.		
13-Feb-04	0188	Information Amendment: Clinical		SP619	Open-label, randomized, single dose study to evaluate the absorption, metabolism, and excretion of [¹⁴ C]-labeled SPM 927 (harkoseride) following oral and intravenous administration to 10 healthy male caucasian subjects		
13-Feb-04	0188	Protocol Amendment: Change in Protocol		SP616	Amendment 1		
13-Feb-04	0188	Response to FDA Request for Information			Schwarz responds to FDA letter 24-dec-2003 regarding epilepsy IV comments and recommendations.		
13-Feb-04	0188	Protocol Amendment: Change in Protocol		SP615	Amendment 5		
18-Feb-04	0189	Initial Safety Report		SP615		2004-00049	11281
18-Feb-04	0190	Response to FDA Request for Information			Respond to FDA letter 3-dec-2003 regarding statistics, biopharm, and pharmacology.		

Monday, November 10, 2008

IND 57,939

Page 51 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Feb-04	0191		Protocol Amendment: New Investigator	SP615	Revised investigators		
24-Feb-04	0192		Follow-up Safety Report	SP615		2003-00474	11503
10-Mar-04	0193		General Correspondence	SP640	Submit pain protocol SP640 to epilepsy INDs for information purposes only.		
18-Mar-04	0194		Protocol Amendment: New Investigator	SP754	New investigators		
18-Mar-04	0194		Protocol Amendment: New Investigator	SP667	Revised investigators		
18-Mar-04	0194		Protocol Amendment: New Investigator	SP615	Revised investigators		
24-Mar-04			FDA Phone Contact		Ms. Griffiths, FDA, returns call requesting comments to proposal for pediatric exclusivity. Ms. Griffiths suggests Schwarz make a proposal the division would review and then pass on to the committee.		
24-Mar-04	0195		Information Amendment: CMC Data		Revised CMC data including description of scale up drug substance synthesis process and revised specifications and analytical methods and stability.		
01-Apr-04	0196		General Correspondence	SP755	Schwarz submits copy of SP755 non-IND protocol for information purposes only.		
01-Apr-04	0197		Initial Safety Report	SP615		2004-00129	11610
01-Apr-04	0197		Initial Safety Report	SP665		2004-00135	10175

Monday, November 10, 2008

IND 57,939

Page 52 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
06-Apr-04	0198		Follow-up Safety Report	SP615		2003-00248	10501
15-Apr-04	0199		Follow-up Safety Report	SP665		2004-00135	10175
19-Apr-04	0200		Protocol Amendment: New Investigator	SP667	Revised investigators		
19-Apr-04	0200		Protocol Amendment: New Investigator	SP754	New investigators		
19-Apr-04	0200		Protocol Amendment: New Investigator	SP615	New investigators		
03-May-04	0201		Initial Safety Report	SP615		2004-00189	10185
12-May-04	0202		Follow-up Safety Report	SP615		2004-00129	11610
13-May-04	0203		Protocol Amendment: New Protocol	SP756	New protocol		
19-May-04	0204	v1 p1	Information Amendment: Pharmacology/Toxicology	E0066	Therapeutic effect of SPM 927 in painful diabetic neuropathy in the rat		
19-May-04	0204	v1 p29	Information Amendment: Clinical	SP587	Single dose tolerance study with ascending oral doses of SPM 927 (harkoseride) in healthy male caucasian volunteers		
19-May-04	0204	v11 p1	Information Amendment: Clinical	SP603	Open-label multiple dose study to evaluate the effect of carbamazepine on the pharmacokinetics of SPM 927 (harkoseride) in 20 healthy male caucasian volunteers		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
19-May-04	0204	v15 p1	Information Amendment: Clinical	SP618	Open-label multiple dose study to evaluate the effect of harkoseride (SPM 927) on the pharmacokinetics of carbamazepine in 20 healthy male caucasian volunteers		
19-May-04	0204	v5 p1	Information Amendment: Clinical	SP602	Open-label randomized, multiple dose, cross-over study to evaluate the pharmacokinetic effect of valproic acid (VPA) on hardoseride (SPM 927) in 16 healthy male caucasian volunteers		
19-May-04	0205		Initial Safety Report	SP615		2004-00232	11478
20-May-04	0206		Protocol Amendment: New Investigator	SP754	New investigators		
20-May-04	0206		Protocol Amendment: New Investigator	SP667	Revised investigators		
20-May-04	0206		Protocol Amendment: New Investigator	SP615	Revised investigator		
27-May-04	0207		Follow-up Safety Report	SP615		2004-00049	11281
02-Jun-04			7-Day Safety Report Fax	SP615	Fax 7-day safety report to Ms. Griffiths, FDA.	2004-00274	11428
02-Jun-04	0208		7-Day Safety Report	SP615		2004-00274	11428
07-Jun-04	0209		Initial Safety Report	SP615		2004-00266	10194
21-Jun-04	0210		Protocol Amendment: New Investigator	SP667	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 54 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
<i>Date</i>	<i>No</i>	<i>Type</i>	<i>Location</i>			<i>Mfr</i>	<i>Control No</i>	
21-Jun-04	0210	Protocol Amendment: New Investigator		SP754	New and revised investigators			
24-Jun-04	0211	Follow-up Safety Report		SP615		2004-00266		10194
24-Jun-04	0211	Follow-up Safety Report		SP615		2004-00274		11428
28-Jun-04	0212	Initial Safety Report		SP743		2004-00321		11406/8011
28-Jun-04	0212	Initial Safety Report		SP742		2004-00326		15502/80010
28-Jun-04	0213	Annual Report			Period covering 19-APR-2004 through 25-MAR-2004			
01-Jul-04		7-Day Safety Report Fax		SP742	Fax 7-day safety reports to FDA	2004-00356		13002/80062
01-Jul-04		7-Day Safety Report Fax		SP743	Fax 7-day safety reports to FDA	2004-00355		12307
01-Jul-04	0214	Follow-up Safety Report		SP615		2004-00232		11478
01-Jul-04	0214	Follow-up Safety Report		SP667		2003-00298		11910/80301
01-Jul-04	0215	Initial Safety Report		SP742		2004-00356		13002/80062
01-Jul-04	0215	7-Day Safety Report		SP743		2004-00355		12307
13-Jul-04	0216	Follow-up Safety Report		SP743		2004-00355		12307/80040
13-Jul-04	0216	Follow-up Safety Report		SP742		2004-00326		15502/80010

Monday, November 10, 2008

IND 57,939

Page 55 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
13-Jul-04	0217		Initial Safety Report	SP743		2004-00366	12302/80036
14-Jul-04			7-Day Safety Report Fax	SP743	Fax Ms. Griffis, FDA, 7-day safety report	2004-00380	15712/80094
14-Jul-04	0218		7-Day Safety Report	SP743		2004-00380	15712/80094
19-Jul-04	0219		Initial Safety Report	SP742		2004-00370	13805/80082
20-Jul-04	0220		Protocol Amendment: New Investigator	SP754	New and revised investigators		
20-Jul-04	0220		Protocol Amendment: New Investigator	SP667	Revised investigators		
20-Jul-04	0220		Protocol Amendment: New Investigator	SP615	New and revised investigators		
21-Jul-04	0221		Information Amendment: Clinical	SP588	Multiple dose tolerance study with ascending oral doses of SPM 927 (harkoseride) in healthy male caucasian volunteers		
21-Jul-04	0222		Follow-up Safety Report	SP742		2004-00356	13002/80062
04-Aug-04			7-Day Safety Report Fax	SP742	Fax Ms. Griffis, FDA, 7-day safety report	2004-00428	14309
04-Aug-04	0223		7-Day Safety Report	SP742		2004-00428	14309
05-Aug-04	0224		Follow-up Safety Report	SP615		2004-00232	11478
05-Aug-04	0224		Follow-up Safety Report	SP615		2004-00266	10194

Monday, November 10, 2008

IND 57,939

Page 56 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
05-Aug-04	0224		Follow-up Safety Report	SP743		2004-00321	11406/80110
05-Aug-04	0224		Follow-up Safety Report	SP743		2004-00380	15712/80094
09-Aug-04			7-Day Safety Report Fax	SP742	Fax Ms. Griffith, FDA, 7-day safety report	2004-00441	15601/80177
09-Aug-04	0225		7-Day Safety Report	SP742		2004-00441	15601/80177
10-Aug-04			FDA Phone Contact	SP742	Dr. Hershkowitz, FDA, calls to request additional information regarding subject no. 13002/80062		13002/80062
10-Aug-04	0226		Information Amendment: Clinical		Revised investigator's brochure dated May 2004		
12-Aug-04			7-Day Safety Report Fax	SP743	Fax Ms. Griffith, FDA, 7-day safety report	2004-00447	17508/80301
12-Aug-04	0227		Follow-up Safety Report	SP742		2004-00428	14309/80133
12-Aug-04	0227		Follow-up Safety Report	SP742		2004-00370	13805/80082
12-Aug-04	0228		7-Day Safety Report	SP743		2004-00447	17508/80301
16-Aug-04	0229		Initial Safety Report	SP743		2004-00443	16811/80194
19-Aug-04	0230		Protocol Amendment: New Investigator	SP754	New investigators		
19-Aug-04	0230		Protocol Amendment: New Investigator	SP615	New investigator		

Monday, November 10, 2008

IND 57,939

Page 57 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
19-Aug-04	0230		Protocol Amendment: New Investigator	SP667	Revised investigators		
23-Aug-04	0231		Follow-up Safety Report	SP743		2004-00443	16811/80194
23-Aug-04	0231		Follow-up Safety Report	SP743		2004-00447	17508/80301
23-Aug-04	0231		Follow-up Safety Report	SP743		2004-00355	12307/80040
23-Aug-04	0231		Follow-up Safety Report	SP615		2003-00323	10616/10538
24-Aug-04			7-Day Safety Report Fax	SP742	Fax Ms. Griffis, FDA 7-day safety report	2004-00483	15210/80059
24-Aug-04	0232		7-Day Safety Report	SP742		2004-00483	15210/80059
25-Aug-04	0233		Response to FDA Request for Information	SP742	Respond to FDA request for follow-up information regarding this case; requested on 10-AUG-2004.	2004-00356	13002/80062
26-Aug-04	0234		General Correspondence		Schwarz requests type B meeting, end of phase 2 to discuss with FDA the available clinical data and the phase 3 development program's acceptability to support a mktg application		
30-Aug-04	0235		Follow-up Safety Report	SP742		2004-00356	13002/80062
30-Aug-04	0235		Follow-up Safety Report	SP742		2004-00370	13805/80082
02-Sep-04			7-Day Safety Report Fax	SP743	Fax Ms. Griffis, FDA, 7-day safety report	2004-00507	14919

Monday, November 10, 2008

IND 57,939

Page 58 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
02-Sep-04	0236		7-Day Safety Report	SP743		2004-00507	14919
03-Sep-04			FDA Phone Contact		Ms. Griffis, FDA, calls to grant end of phase 2 meeting on 3-NOV-2004.		
07-Sep-04			FDA Correspondence		Ms. Griffis, FDA, emails confirmation of end of phase 2 meeting 3-NOV-2004.		
09-Sep-04	0237		Follow-up Safety Report	SP743		2004-00447	17508/80301
09-Sep-04	0237		Follow-up Safety Report	SP615		2004-00274	11428
09-Sep-04	0237		Follow-up Safety Report	SP743		2004-00443	16811/80194
17-Sep-04	0238		Protocol Amendment: New Investigator	SP667	Revised investigators		
17-Sep-04	0238		Protocol Amendment: New Investigator	SP754	New investigators		
17-Sep-04	0238		Protocol Amendment: New Investigator	SP615	Revised investigator		
23-Sep-04			7-Day Safety Report	SP742	Fax Ms. Griffis, FDA, 7-day safety report	2004-00553	13308/80166
23-Sep-04	0239		7-Day Safety Report	SP742		2004-00553	13308/80166
27-Sep-04	0240		Initial Safety Report	SP742		2004-00551	14609
27-Sep-04	0240		Initial Safety Report	SP742		2004-00544	15803

Monday, November 10, 2008

IND 57,939

Page 59 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
28-Sep-04	0241		Meeting Package		End of phase 2 meeting package to discuss proposed phase 3 development on 3-NOV-2004.		
29-Sep-04	0242		Follow-up Safety Report	SP743		2004-00507	14919
29-Sep-04	0242		Follow-up Safety Report	SP742		2004-00428	14309/80133
29-Sep-04	0242		Follow-up Safety Report	SP743		2004-00443	16811/80194
08-Oct-04	0243		Initial Safety Report	SP615		2004-00573	10529
13-Oct-04			7-Day Safety Report	SP615	Fax Ms. Griffis, FDA, 7-day safety report	2004-00580	10626
13-Oct-04	0244		7-Day Safety Report	SP615		2004-00580	10626
15-Oct-04			7-Day Safety Report	SP754	Fax Ms. Griffis, FDA, 7-day safety report	2004-00616	15605
15-Oct-04	0245		7-Day Safety Report	SP754		2004-00616	15605
19-Oct-04	0246		Follow-up Safety Report	SP742		2004-00551	14609
19-Oct-04	0246		Follow-up Safety Report	SP754		2004-00616	15605
19-Oct-04	0246		Follow-up Safety Report	SP742		2004-00553	13308/80166
19-Oct-04	0246		Follow-up Safety Report	SP615		2004-00573	10529
19-Oct-04	0246		Follow-up Safety Report	SP742		2004-00544	15803

Monday, November 10, 2008

IND 57,939

Page 60 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Oct-04	0247		Protocol Amendment: New Investigator	SP667	Revised investigators		
20-Oct-04	0247		Protocol Amendment: New Investigator	SP756	New investigators		
20-Oct-04	0247		Protocol Amendment: New Investigator	SP754	New investigators		
25-Oct-04	0248		Initial Safety Report	SP743		2004-00614	17603/80422
25-Oct-04	0249		Information Amendment: CMC Data		Submits revised information on drug substance and drug product		
01-Nov-04			FDA Correspondence		Ms. Griffis, FDA, emails CMC responses to questions from the end of phase 2 briefing document.		
01-Nov-04	0250		Follow-up Safety Report	SP743		2004-00380	15712/80094
04-Nov-04			FDA Correspondence		Ms. Griffis, FDA, emails she will send the FDA attendees list tomorrow.		
04-Nov-04			General Correspondence		Email Ms. Griffis, FDA, request for list of names of FDA attendees for end of phase 2 meeting.		
04-Nov-04			FDA Correspondence		Ms. Griffis, FDA, emails will be in touch.		
04-Nov-04			General Correspondence		Schwarz emails confirmation of email CMC responses was received.		
05-Nov-04			FDA Correspondence		Ms. Griffis, FDA, emails list of FDA attendees.		

Monday, November 10, 2008

IND 57,939

Page 61 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
08-Nov-04			7-Day Safety Report	SP742	Fax Ms. Griffiths, FDA, 7-day safety report	2004-00599	14004/80152
08-Nov-04	0251		7-Day Safety Report	SP742		2004-00599	14004/80152
10-Nov-04	0252		Initial Safety Report	SP615		2004-00665	10402
12-Nov-04	0253		Follow-up Safety Report	SP742		2004-00551	14609
12-Nov-04	0253		Follow-up Safety Report	SP742		2004-00441	15601/80177
12-Nov-04	0253		Follow-up Safety Report	SP742		2004-00326	15502/80010
15-Nov-04			General Correspondence		Email Ms. Griffiths, FDA, to see if she has spoken with pharm/tox reviewers regarding point to consider document for juv tox.		
16-Nov-04			FDA Correspondence		Ms. Griffiths, FDA, emails that pharm/tox reviewers should have a response today.		
16-Nov-04			FDA Correspondence		Ms. Griffiths, FDA, emails juv tox recommendations from FDA pharm/tox reviewers.		
17-Nov-04	0254		SB Meeting Minutes		Schwarz submits end of phase 2 meeting minutes from 3-NOV-2004.		
19-Nov-04	0255		Protocol Amendment: New Investigator	SP756	New investigators		
19-Nov-04	0255		Protocol Amendment: New Investigator	SP667	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 62 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
19-Nov-04	0255		Protocol Amendment: New Investigator	SP615	New and revised investigators		
19-Nov-04	0255		Protocol Amendment: New Investigator	SP754	New and revised investigators		
29-Nov-04	0256		Follow-up Safety Report	SP742		2004-00483	15210/80059
01-Dec-04			FDA Meeting Minutes		Ms. Griffiths, FDA, emails end of phase 2 meeting minutes from 3-NOV-2004.		
01-Dec-04	0257		Follow-up Safety Report	SP742		2004-00553	13308/80166
01-Dec-04	0257		Follow-up Safety Report	SP743		2004-00614	17603/80422
07-Dec-04	0258		Response to FDA Request for Information		Schwarz sends questions to FDA CMC responses from end of phase 2 briefing document.		
07-Dec-04	0259		Initial Safety Report	SP743		2004-00742	17029/80430
15-Dec-04	0260		Follow-up Safety Report	SP615		2004-00665	10402
20-Dec-04	0261		Protocol Amendment: New Investigator	SP754	New and revised investigator		
20-Dec-04	0261		Protocol Amendment: New Investigator	SP756	New investigators		
21-Dec-04			7-Day Safety Report	SP768	Fax Ms. Griffiths, FDA, 7-day safety report	2004-00790	112104/80001
21-Dec-04			7-Day Safety Report	SP742	Fax Ms. Griffiths, FDA, 7-day safety report	2004-00791	14806/80389

Monday, November 10, 2008

IND 57,939

Page 63 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
21-Dec-04	0262		7-Day Safety Report	SP768		2004-00790	112104/80001
21-Dec-04	0262		7-Day Safety Report	SP742		2004-00791	14806/80389
22-Dec-04	0263		Follow-up Safety Report	SP743		2004-00742	17029/80430
22-Dec-04	0264		Initial Safety Report	SP746		2004-00778	17514
22-Dec-04	0264		Initial Safety Report	SP755		2004-00785	11601/85761
28-Dec-04			7-Day Safety Report	SP755	Fax Ms. Griffiths, FDA, 7-day safety report	2004-00815	106302/82234
28-Dec-04	0265		7-Day Safety Report	SP755		2004-00815	106302/82234
03-Jan-05	0266		Follow-up Safety Report	SP755		2004-00785	11601/85761
03-Jan-05	0266		Follow-up Safety Report	SP743		2004-00742	17029/80430
03-Jan-05	0266		Follow-up Safety Report	SP615		2004-00580	10626
05-Jan-05	0267		Request FDA Comment	LPT 18602/04	Submit draft nonclinical protocols for FDA review and comment		
05-Jan-05	0267		Request FDA Comment	LPT 18601/04	Submit draft nonclinical protocols for FDA review and comment		
10-Jan-05	0268		Follow-up Safety Report	SP742		2004-00599	14004/80152
10-Jan-05	0268		Follow-up Safety Report	SP746		2004-00778	17514

Monday, November 10, 2008

IND 57,939

Page 64 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
10-Jan-05	0268		Follow-up Safety Report	SP755		2004-00785	11601/85761
10-Jan-05	0268		Follow-up Safety Report	SP768		2004-00790	112104/80001
13-Jan-05			7-Day Safety Report	SP755	Fax Ms. Griffis, FDA, 7-day safety report	2005-00008	122303/87995
13-Jan-05	0269		7-Day Safety Report	SP755		2005-00008	122303/87995
20-Jan-05			7-Day Safety Report	SP742	Fax Ms. Griffis, FDA, 7-day safety report	2005-00051	14243/80369
20-Jan-05	0270		Initial Safety Report	SP755		2005-00015	110902/83890
20-Jan-05	0271		7-Day Safety Report	SP742		2005-00051	14243/80369
24-Jan-05	0272		7-Day Safety Report	SP742		2005-00041	10911/80361
24-Jan-05	0272		7-Day Safety Report	SP742		2005-00059	12725/80373
24-Jan-05	0273		Protocol Amendment: New Investigator	SP754	New investigators		
24-Jan-05	0273		Protocol Amendment: New Investigator	SP756	New investigators		
25-Jan-05			7-Day Safety Report	SP768	Fax Ms. Griffis, FDA, 7-day safety report	2005-00060	111305/80162
25-Jan-05			7-Day Safety Report	SP768	Fax Ms. Griffis, FDA, 7-day safety report	2005-00061	111307/80163
25-Jan-05	0274		7-Day Safety Report	SP768		2005-00060	111305/80162

Monday, November 10, 2008

IND 57,939

Page 65 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
25-Jan-05	0274		7-Day Safety Report	SP768		2005-00061	111307/80163
27-Jan-05	0275		Follow-up Safety Report	SP755		2005-00008	122303/87995
28-Jan-05	0276		Initial Safety Report	SP755		2005-00049	118603/86661
01-Feb-05			7-Day Safety Report	SP742	Fax Ms. Griffis, FDA, 7-day safety report	2005-00088	14251/80421
01-Feb-05			7-Day Safety Report	SP755	Fax Ms. Griffis, FDA, 7-day safety report	2005-00077	10841/82989
01-Feb-05	0277		7-Day Safety Report	SP755		2005-00077	10841/82989
01-Feb-05	0277		7-Day Safety Report	SP742		2005-00088	14251/80421
02-Feb-05			FDA Correspondence		Ms. Griffis, FDA, will check on review status of juv tox protocol and requests two desk copies of the drug interaction study request.		
02-Feb-05			General Correspondence		Email Ms. Griffis, FDA, a request for FDA comment will be sent regarding justification for no more drug interaction studies to be conducted. Requests update on juv tox protocol comments.		
02-Feb-05	0278		Follow-up Safety Report	SP755		2004-00785	116101/85761
02-Feb-05	0278		Follow-up Safety Report	SP755		2005-00015	110902/83890
02-Feb-05	0278		Follow-up Safety Report	SP768		2005-00060	111305/80162

Monday, November 10, 2008

IND 57,939

Page 66 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
02-Feb-05	0278		Follow-up Safety Report	SP768		2005-00061	111307/80163
03-Feb-05			FDA Correspondence		Ms. Griffis, FDA, sends comments to review of draft protocol LPT 18602/04, a juvenile rat toxicology study.		
03-Feb-05	0279		Request FDA Comment		Schwarz requests FDA concurrence that no additional drug interaction trials are required		
04-Feb-05			7-Day Safety Report	SP768	Fax Ms. Griffis, FDA, 7-day safety report	2005-00096	112703/80093
04-Feb-05	0280		7-Day Safety Report	SP768		2005-00096	112703/80093
04-Feb-05	0281		Follow-up Safety Report	SP742		2005-00041	10911/80361
04-Feb-05	0281		Follow-up Safety Report	SP742		2005-00051	14243/80369
04-Feb-05	0281		Follow-up Safety Report	SP742		2005-00059	12725/80373
09-Feb-05			7-Day Safety Report	SP768	Fax Ms. Griffis, FDA, 7-day safety report	2005-00119	110403/80108
09-Feb-05	0282		7-Day Safety Report	SP768		2005-00119	110403/80108
09-Feb-05	0283		Follow-up Safety Report	SP755		2005-00049	118603/86661
10-Feb-05	0284		Protocol Amendment: Change in Protocol	SP754	Amendment 1		
10-Feb-05	0284		Other	SP755	Amendment 1 for non-IND protocol SP755		

Monday, November 10, 2008

IND 57,939

Page 67 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
10-Feb-05	0285		Initial Safety Report	SP768		2005-00089	112909/80024
10-Feb-05	0285		Initial Safety Report	SP754		2004-00454	15103/80069
14-Feb-05	0286		Follow-up Safety Report	SP742		2005-00088	14251/80421
14-Feb-05	0286		Follow-up Safety Report	SP742		2004-00791	14806/80389
14-Feb-05	0286		Follow-up Safety Report	SP615		2004-00580	10626
14-Feb-05	0286		Follow-up Safety Report	SP755		2005-00077	108401/82989
14-Feb-05	0286		Follow-up Safety Report	SP768		2005-00096	112703/80093
15-Feb-05	0287		Follow-up Safety Report	SP615		2004-00189	10185
17-Feb-05	0288		Protocol Amendment: New Investigator	SP754	Revised investigators		
17-Feb-05	0288		Protocol Amendment: New Investigator	SP756	New and revised investigators		
22-Feb-05	0289		Other		Schwarz responds to FDA end of phase 2 meeting minutes, 3-NOV-2004, regarding rat study 1108-003P and rabbits 1108-002P dose shows adequate maternal toxicity and request FDA agreement		
24-Feb-05			FDA Phone Contact		Schwarz calls Ms. Griffiths, FDA, to discuss timing of proposed pediatric study request.		

Monday, November 10, 2008

IND 57,939

Page 68 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
24-Feb-05	0290		Initial Safety Report	SP615		2004-00732	11280
24-Feb-05	0290		Initial Safety Report	SP754		2005-00160	16102/80118
01-Mar-05			7-Day Safety Report	SP746	Fax Ms. Griffiths, FDA, 7-day safety report	2005-00170	14913
01-Mar-05			7-Day Safety Report	SP745	Fax Ms. Griffiths, FDA, 7-day safety report	2005-00168	175210
01-Mar-05	0291		7-Day Safety Report	SP745		2005-00168	175210
01-Mar-05	0291		7-Day Safety Report	SP746		2005-00170	14913
03-Mar-05			FDA Correspondence		Ms. Griffiths, FDA, emails to agree with our proposal for no additional drug interaction studies to be conducted.		
03-Mar-05	0292		Follow-up Safety Report	SP742		2005-00041	10911/80361
03-Mar-05	0292		Follow-up Safety Report	SP754		2004-00454	15103/80069
04-Mar-05	0293		7-Day Safety Report	SP755		2005-00185	116407/85873
08-Mar-05	0294		Initial Safety Report	SP756		2005-00177	15103
09-Mar-05	0295		7-Day Safety Report	SP742		2005-00193	12204/80337
11-Mar-05	0296		Initial Safety Report	SP743		2004-00444	17805/80350
14-Mar-05	0297		Follow-up Safety Report	SP754		2005-00160	16102/80118

Monday, November 10, 2008

IND 57,939

Page 69 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
14-Mar-05	0297		Follow-up Safety Report	SP745		2005-00168	175210
15-Mar-05	0298		Response to FDA Request for Information	SP588	Schwarz responds to FDA request for additional information on the toxic hepatitis case no. 2000-00026	2000-00026	10215/8061
16-Mar-05			FDA Correspondence		FDA requests Schwarz identify placebo-controlled trials and identify possibly suicide related AEs.		
18-Mar-05	0299		Protocol Amendment: New Investigator	SP754	New and revised investigators		
18-Mar-05	0299		Protocol Amendment: New Investigator	SP756	New and revised investigators		
18-Mar-05	0299		Protocol Amendment: New Investigator	SP667	Revised investigators		
18-Mar-05	0299		Protocol Amendment: New Investigator	SP615	Revised investigator		
21-Mar-05	0300		Follow-up Safety Report	SP768		2005-00089	112909/80024
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00380	15712/80094
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00447	17508/80301
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00321	11406/80110
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00366	12302/80036

Monday, November 10, 2008

IND 57,939

Page 70 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00443	16811/80194
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00742	17029/80430
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00355	12307/80040
23-Mar-05	0301		Follow-up Safety Report	SP743		2004-00507	14919/80387
29-Mar-05	0302		Follow-up Safety Report	SP755		2005-00077	108401/82989
29-Mar-05	0302		Follow-up Safety Report	SP742		2005-00193	12204/80337
01-Apr-05	0303		Follow-up Safety Report	SP755		2005-00185	116407/85873
01-Apr-05	0303		Follow-up Safety Report	SP768		2005-00119	110403/80108
01-Apr-05	0303		Follow-up Safety Report	SP665		2002-00306	10141/10141
04-Apr-05	0304		Initial Safety Report	SP615		2005-00253	10476
12-Apr-05	0305		Follow-up Safety Report	SP746		2005-00170	14913
14-Apr-05	0306		Follow-up Safety Report	SP755		2005-00008	122303/87995
14-Apr-05	0306		Follow-up Safety Report	SP742		2004-00428	14309/80133
20-Apr-05	0307		Protocol Amendment: New Investigator	SP756	New and revised investigators		

Monday, November 10, 2008

IND 57,939

Page 71 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Apr-05	0307		Protocol Amendment: New Investigator	SP754	Revised investigator		
25-Apr-05	0308		Follow-up Safety Report	SP756		2005-00177	15103
25-Apr-05	0308		Follow-up Safety Report	SP746		2005-00170	14913
26-Apr-05	0309		Initial Safety Report	SP768		2005-00303	101803/80331
27-Apr-05	0310		Protocol Amendment: Change in Protocol	SP756	Amendment 1		
27-Apr-05	0310		Protocol Amendment: Change in Protocol	SP615	Amendment 6		
27-Apr-05	0310		Protocol Amendment: Change in Protocol	SP615	Amendment 7		
02-May-05	0311		Follow-up Safety Report	SP768		2005-00119	110403/80109
02-May-05	0311		Follow-up Safety Report	SP768		2005-00303	101803/80331
02-May-05	0312		7-Day Safety Report	SP755		2005-00323	106406/82279
11-May-05	0313		Initial Safety Report	SP830		2005-00326	110503
11-May-05	0313		Initial Safety Report	SP754		2005-00341	16013/80206
18-May-05	0314		Follow-up Safety Report	SP615		2005-00253	10476

Monday, November 10, 2008

IND 57,939

Page 72 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>		<i>Title/ Description</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>		<i>Title/ Description</i>		<i>Mfr</i>	<i>Control No</i>	<i>Subject No</i>	
19-May-05	0315		Other			Response to end of phase 2 meeting minutes with summary and analysis of cases of abnormal liver function					
19-May-05	0316		Protocol Amendment: New Investigator	SP754		New investigators					
19-May-05	0316		Protocol Amendment: New Investigator	SP756		New investigators					
19-May-05	0316		Protocol Amendment: New Investigator	SP615		Revised investigator					
20-May-05			7-Day Safety Report	SP768		Fax Ms. Griffis, FDA, 7-day safety report		2005-00375		109308/80117	
20-May-05	0317		7-Day Safety Report	SP768				2005-00375		109308/80117	
24-May-05	0318		Initial Safety Report	SP768				2005-00358		108702/80471	
24-May-05	0318		Initial Safety Report	SP754				2005-00370		12804/80207	
26-May-05	0319		Information Amendment: Pharmacology/Toxicology	LPT 13124/00		104-week carcinogenicity study of SPM 927 by oral administration to CD-1 mice					
26-May-05	0319		Information Amendment: Pharmacology/Toxicology	LPT 13295/00		104-week carcinogenicity study of SPM 927 by oral administration to CD-1 rats					
27-May-05			7-Day Safety Report	SP746		Fax Ms. Griffis, FDA, 7-day safety report		2005-00011		15009	
27-May-05	0320		Follow-up Safety Report	SP742				2005-00193		12204/80337	
27-May-05	0320		Follow-up Safety Report	SP755				2005-00077		108401/82989	

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
27-May-05	0321		7-Day Safety Report	SP746		2005-00011	15009
02-Jun-05	0322		Information Amendment: Clinical	SP607	An open label, dose titration trial to determine tolerability and efficacy of oral SPM 927 as adjunctive therapy in patients with partial seizures with or without secondary generalization		
03-Jun-05	0323		Initial Safety Report	SP746		2005/00409	17014
03-Jun-05	0323		Initial Safety Report	SP755		2005-00405	110109/83605
06-Jun-05	0324		7-Day Safety Report	SP768		2005-00424	101410/80256
06-Jun-05	0325		Follow-up Safety Report	SP755		2005-00323	106406/82279
07-Jun-05			FDA Correspondence		Ms. Griffiths, FDA, provides contact information for Ms. Calder during her leave of absence		
07-Jun-05	0326		Request FDA Comment		Submit rationale for proposed LPT 18602/04 juvenile tox study, draft summary of dose range finding study LPT 18601/04, revised draft protocol for repeated dose juvenile tox study and tabulated summaries of tox studies		
15-Jun-05	0327		7-Day Safety Report	SP768		2005-00444	112305/80382
16-Jun-05	0328		Protocol Amendment: New Investigator	SP640	New investigator		
16-Jun-05	0328		Protocol Amendment: New Protocol	SP640	New protocol		

Monday, November 10, 2008

IND 57,939

Page 74 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
20-Jun-05	0329		Information Amendment: Clinical	SP667	A multicenter, double-blind, randomized, placebo-controlled, parallel group trial to investigate the efficacy and safety of SPM 927 (200mg/day, 400 mg/day, 600mg/day) as adjunctive therapy in subj. with partial seizures w/ or w/o secondary generalization		
22-Jun-05	0330		Follow-up Safety Report	SP615		2004-00580	10626
23-Jun-05	0331		Request FDA Comment		Request bio waiver for in vivo bioequivalence study for syrup; submit core text of SP643 and SP658		
23-Jun-05	0332		Initial Safety Report	SP746		2005-00441	17415
24-Jun-05	0333		Follow-up Safety Report	SP768		2005-00424	101410/80256
24-Jun-05	0333		Follow-up Safety Report	SP768		2005-00375	109308/80117
24-Jun-05	0333		Follow-up Safety Report	SP755		2005-00405	110109/83605
24-Jun-05	0333		Follow-up Safety Report	SP746		2005-00409	17014
24-Jun-05	0334		Protocol Amendment: New Investigator	SP615	Revised investigators		
24-Jun-05	0334		Protocol Amendment: New Investigator	SP756	New and revised investigators		
24-Jun-05	0334		Protocol Amendment: New Investigator	SP754	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 75 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
27-Jun-05	0335		Initial Safety Report	SP756		2005-00467	16005
27-Jun-05	0335		Initial Safety Report	SP615		2005-00465	10477
27-Jun-05	0335		Initial Safety Report	SP755		2005-00206	108202/82918
30-Jun-05	0336		Annual Report		period covering 26-MAR-2004 through 25-MAR-2005		
01-Jul-05	0337	v1 p1	Information Amendment: Clinical	678-02	Determination of SPM 927 and SPM 12809 in human plasma by HPLC Electrospray MS/MS after oral administration of SPM 927 and metformin to healthy male subjects (SP660)		
01-Jul-05	0337	v1 p136	Information Amendment: Clinical	679-02	Determination of SPM 927 and SPM 12809 in human urine by HPLC Electrospray MS/MS after oral administration of SPM 927 and metformin to healthy male subjects (SP660)		
01-Jul-05	0337	v2 p1	Information Amendment: Clinical	680-02	Determination of SPM 927 and SPM 12809 in human saliva by HPLC Electrospray MS/MS after oral administration of SPM 927 and metformin to healthy male subjects (SP660)		
01-Jul-05	0337	v2 p64	Information Amendment: Clinical	031/04-05.MN	Validation of a LC/MS/MS method for the determination of metformin concentrations in human plasma and human urine samples and application of the validated assays to routine analysis of plasma and urine samples of study SP660		

Monday, November 10, 2008

IND 57,939

Page 76 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
06-Jul-05	0338		Follow-up Safety Report	SP756		2005-00467	16005
06-Jul-05	0338		Follow-up Safety Report	SP768		2005-00424	101410/80256
06-Jul-05	0338		Follow-up Safety Report	SP768		2005-00444	112305/80382
07-Jul-05	0339		Information Amendment: Pharmacology/Toxicology	750-03	Determination of SPM 927 and SPM 12809 in rat plasma by HPLC electrospray MS after oral administration of lacosamide to juvenile rats in a dose-range-finding study (LPT 18601/04)		
08-Jul-05	0340		Information Amendment: Clinical	SP642	Open, non-randomized, group comparison to investigate the pharmacokinetics, safety, and tolerability of 100mg SPM 927 twice daily in male and female subjects with hepatic impairment compared w/ male and female healthy subj following multiple-dose admin		
11-Jul-05			FDA Correspondence		FDA mails clarification letter to respond to a number of questions as a result of agency letter 16-MAR-2005 requesting possibly suicide related evaluation of AEs occurring in lacosamide trials		
12-Jul-05			FDA Correspondence		FDA faxes clarification letter to respond to a number of questions as a result of agency letter 16-MAR-2005 requesting possibly suicide related evaluation of AEs occurring in lacosamide trials		
14-Jul-05	0341		Initial Safety Report	SP755		2005-00493	106305/82237

Monday, November 10, 2008

IND 57,939

Page 77 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
14-Jul-05	0342		Follow-up Safety Report	SP615		2004-00580	10626
14-Jul-05	0342		Follow-up Safety Report	SP754		2005-00341	16013/80206
14-Jul-05	0342		Follow-up Safety Report	SP768		2005-00375	109308/80117
18-Jul-05			7-Day Safety Report	SP830	Fax Ms. Griffiths, FDA, 7-day safety report	2005-00211	108301
18-Jul-05	0343		Initial Safety Report	SP756		2005-00512	15001
18-Jul-05	0343		Initial Safety Report	SP830		2005-00492	112007
18-Jul-05	0344		7-Day Safety Report	SP830		2005-00211	108301
20-Jul-05	0345		Protocol Amendment: New Investigator	SP615	Revised investigators		
20-Jul-05	0345		Protocol Amendment: New Investigator	SP756	New and revised investigators		
20-Jul-05	0345		Protocol Amendment: New Investigator	SP754	New and revised investigators		
20-Jul-05	0346		Follow-up Safety Report	SP830		2005-00492	112007
21-Jul-05	0347		Follow-up Safety Report	SP768		2005-00444	112305/80382
21-Jul-05	0347		Follow-up Safety Report	SP746		2005-00441	17415
21-Jul-05	0347		Follow-up Safety Report	SP755		2005-00493	106305/82237

Monday, November 10, 2008

IND 57,939

Page 78 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS</i>
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr</i>	<i>Control No</i>	
25-Jul-05	0348		7-Day Safety Report	SP768			2005-00545	108808/80185
27-Jul-05	0349		Information Amendment: Clinical	SP586	A phase II, multicenter, ascending dose assessment of the safety, tolerability, compatibility, efficacy, and pharmacokinetics of harkoseride (ADD 234037) as adjunctive therapy in patients with partial seizures			
28-Jul-05	0350		Follow-up Safety Report	SP742			2005-00193	12204/80337
28-Jul-05	0350		Follow-up Safety Report	SP742			2004-00599	14004/80152
28-Jul-05	0350		Follow-up Safety Report	SP742			2004-00791	14806/80389
28-Jul-05	0350		Follow-up Safety Report	SP742			2005-00041	10911/80361
28-Jul-05	0350		Follow-up Safety Report	SP742			2005-00051	14243/80369
28-Jul-05	0350		Follow-up Safety Report	SP742			2004-00553	13308/80166
28-Jul-05	0350		Follow-up Safety Report	SP742			2005-00088	14251/80421
28-Jul-05	0350		Follow-up Safety Report	SP742			2004-00428	14309/80133
28-Jul-05	0350		Follow-up Safety Report	SP742			2005-00059	12725/80373
28-Jul-05	0350		Follow-up Safety Report	SP742			2004-00551	14609/80056
28-Jul-05	0350		Follow-up Safety Report	SP742			2004-00544	15803/80047

Monday, November 10, 2008

IND 57,939

Page 79 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
28-Jul-05	0350		Follow-up Safety Report	SP742		2004-00441	15601/80177
28-Jul-05	0350		Follow-up Safety Report	SP742		2004-00370	13805/80082
28-Jul-05	0350		Follow-up Safety Report	SP742		2004-00356	13002/80062
28-Jul-05	0350		Follow-up Safety Report	SP742		2004-00326	15502/80010
28-Jul-05	0350		Follow-up Safety Report	SP742		2004-00483	15210/80059
28-Jul-05	0351		Follow-up Safety Report	SP756		2005-00512	15001
29-Jul-05	0352		7-Day Safety Report	SP768		2005-00556	106313/80468
29-Jul-05	0352		7-Day Safety Report	SP768		2005-00552	102704
29-Jul-05	0353		Initial Safety Report	SP768		2005-00533	103902
29-Jul-05	0353		Initial Safety Report	SP768		2005-00544	114721/80494
05-Aug-05	0354		Follow-up Safety Report	SP768		2005-00545	108808/80185
05-Aug-05	0354		Follow-up Safety Report	SP768		2005-00556	106313/80468
05-Aug-05	0354		Follow-up Safety Report	SP830		2005-00211	108301
10-Aug-05	0355		Initial Safety Report	SP746		2005-00503	13706

Monday, November 10, 2008

IND 57,939

Page 80 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
10-Aug-05	0356	v1 p1	Information Amendment: Pharmacology/Toxicology	668	Evaluation of the in vivo metabolism of SPM 927 to SPM 12809 in mice, rats and dogs following repeated oral administration of SPM 927		
10-Aug-05	0356	v1 p139	Information Amendment: Pharmacology/Toxicology	688	Investigation of the metabolism of SPM 927 in different in vitro models		
10-Aug-05	0356	v1 p197	Information Amendment: Pharmacology/Toxicology	0699/025	(14C)-SPM 927: Metabolism in hepatocytes isolated from mouse, rat, rabbit, dog and man		
10-Aug-05	0356	v2 p1	Information Amendment: Pharmacology/Toxicology	728	Assessment of the systemic exposure to SPM 927, its desmethyl and its desacetyl metabolite in a single dose pharmacokinetic study of SPM 927 in male mice (188447/04, LPT)		
10-Aug-05	0356	v2 p144	Information Amendment: Pharmacology/Toxicology	LPT 18772/05	Determination of SPM 927, desmethyl-SPM 927 and desacetyl-SPM 927 concentrations in mouse plasma		
10-Aug-05	0356	v2 p18	Information Amendment: Pharmacology/Toxicology	LPT 18447/04	Single dose pharmacokinetics of SPM 927 in CD@-1 mice		
10-Aug-05	0356	v3 p1	Information Amendment: Pharmacology/Toxicology	0699/023	(14C)-SPM 927: A study of absorption, metabolism and excretion following single and multiple oral administration to the rat		
10-Aug-05	0356	v3 p176	Information Amendment: Pharmacology/Toxicology	750-03	Determination of SPM 927 and SPM 12809 in rat plasma by HPLC- Electrospray MS after oral administration of lacosamide to juvenile rats in a dose-range-finding study (LPT 18601/04)		

Monday, November 10, 2008

IND 57,939

Page 81 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
15-Aug-05	0357		Information Amendment: Clinical	606-03	Re-validation of a solid-phase radioimmunoassay for determination of digoxin in human serum		
15-Aug-05	0357		Information Amendment: Clinical	607-03	Re-validation of a solid-phase radioimmunoassay for determination of digoxin in human urine		
15-Aug-05	0357		Information Amendment: Clinical	682-03	Determination of SPM 927 in human plasma by HPLC Electrospray MS/MS after oral administration of SPM 927 (SP690)		
15-Aug-05	0357		Information Amendment: Clinical	651	Transport of SPM 927 across Caco-2 monolayer-Investigation of P-glycoprotein involvement	2005-00597	111308
15-Aug-05	0358		7-Day Safety Report	SP745			
17-Aug-05	0359		Follow-up Safety Report	SP768		2005-00545	108808/80185
17-Aug-05	0359		Follow-up Safety Report	SP768		2005-00556	106313/80468
17-Aug-05	0359		Follow-up Safety Report	SP746		2005-00441	17415
19-Aug-05	0360		Protocol Amendment: New Investigator	SP754	New investigators		
19-Aug-05	0360		Protocol Amendment: New Investigator	SP615	New and revised investigators		
19-Aug-05	0361		Follow-up Safety Report	SP830		2005-00211	108301

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>Sub Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>
22-Aug-05	0362		Initial Safety Report		SP615		2004-00543	10628
24-Aug-05	0363		Initial Safety Report		SP830		2005-00619	105619
24-Aug-05	0363		Initial Safety Report		SP755		2005-00602	124609/88827
24-Aug-05	0363		Initial Safety Report		SP745		2005-00527	170412
25-Aug-05	0364		7-Day Safety Report		SP745		2005-00626	172706
26-Aug-05	0365		Follow-up Safety Report		SP768		2005-00552	102704
29-Aug-05	0366		7-Day Safety Report		SP768		2005-00634	104610/80545
01-Sep-05	0367		Follow-up Safety Report		SP745		2005-00626	172706
01-Sep-05	0367		Follow-up Safety Report		SP830		2005-00619	105619
01-Sep-05	0368		Initial Safety Report		SP745		2005-00631	111607
01-Sep-05	0368		Initial Safety Report		SP756		2005-00635	11501
08-Sep-05	0369		Initial Safety Report		SP768		2005-00643	109138
08-Sep-05	0369		Initial Safety Report		SP640		2005-00636	82043
08-Sep-05	0370		Follow-up Safety Report		SP755		2005-00323	106406/82279
08-Sep-05	0370		Follow-up Safety Report		SP746		2005-00503	13706

Monday, November 10, 2008

IND 57,939

Page 83 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
08-Sep-05	0370		Follow-up Safety Report	SP745		2005-00631	111607
08-Sep-05	0370		Follow-up Safety Report	SP745		2005-00626	172706
13-Sep-05	0371		7-Day Safety Report	SP863		2005-00662	80011/80011
13-Sep-05	0372		Initial Safety Report	SP756		2005-00649	12603
19-Sep-05	0373		Follow-up Safety Report	SP830		2005-00619	105619
19-Sep-05	0373		Follow-up Safety Report	SP768		2005-00634	104610/80545
19-Sep-05	0373		Follow-up Safety Report	SP755		2005-00206	108202/82918
19-Sep-05	0373		Follow-up Safety Report	SP756		2005-00635	11501
20-Sep-05			General Correspondence		Schwarz writes to Dr. Karet, USAN, and requests corrections to the chemical name and chemical structure for lacosamide		
20-Sep-05	0374		Information Amendment: Clinical	SP645	Randomized, open-label, single-dose, 2-way crossover trial to compare the pharmacokinetics of SPM 927 when given as intravenous solution or as oral tablet in healthy male subjects		
20-Sep-05	0375		Protocol Amendment: New Investigator	SP754	New and revised investigators		
20-Sep-05	0375		Protocol Amendment: New Investigator	SP756	New investigators		

Monday, November 10, 2008

IND 57,939

Page 84 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>				<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Sep-05	0375		Protocol Amendment: New Investigator		SP615	Revised investigators		
26-Sep-05	0376		Follow-up Safety Report		SP768		2005-00544	114721/80494
26-Sep-05	0376		Follow-up Safety Report		SP768		2005-00643	109138
26-Sep-05	0376		Follow-up Safety Report		SP768		2005-00358	108702/80471
29-Sep-05	0377		Initial Safety Report		SP774		2005-00648	104109
03-Oct-05	0378		Follow-up Safety Report		SP756		2005-00649	12603
03-Oct-05	0378		Follow-up Safety Report		SP768		2005-00552	102704
03-Oct-05	0378		Follow-up Safety Report		SP756		2005-00467	16005
11-Oct-05	0379		Follow-up Safety Report		SP745		2005-00527	170412
11-Oct-05	0379		Follow-up Safety Report		SP746		2005-00503	13706
11-Oct-05	0379		Follow-up Safety Report		SP755		2005-00602	124609/88827
11-Oct-05	0379		Follow-up Safety Report		SP756		2005-00635	11501
11-Oct-05	0379		Follow-up Safety Report		SP830		2005-00492	112007
13-Oct-05	0380		Initial Safety Report		SP830		2005-00645	111205

Monday, November 10, 2008

IND 57,939

Page 85 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Oct-05	0381		Protocol Amendment: New Investigator	SP754	New investigators		
20-Oct-05	0381		Protocol Amendment: New Investigator	SP756	New and revised investigators		
26-Oct-05	0382		Follow-up Safety Report	SP755		2005-00206	108202/82918
26-Oct-05	0382		Follow-up Safety Report	SP830		2005-00492	112007
28-Oct-05	0383		7-Day Safety Report	SP768		2005-00744	108217/80452
01-Nov-05	0384		Follow-up Safety Report	SP755		2005-00323	106406/82279
03-Nov-05	0385		Initial Safety Report	SP615		2005-00738	11614
08-Nov-05	0386		Initial Safety Report	SP615		2003-00367	11776
08-Nov-05	0386		Initial Safety Report	SP768		2005-00750	104214
08-Nov-05	0387		Follow-up Safety Report	SP830		2005-00645	111205
10-Nov-05	0388		General Correspondence		Notify FDA of change in address and fax number		
16-Nov-05	0389		Follow-up Safety Report	SP830		2005-00492	112007
16-Nov-05	0389		Follow-up Safety Report	SP745		2005-00597	111308
18-Nov-05	0390		Protocol Amendment: New Investigator	SP754	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 86 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>CIOMS Subject No</i>			<i>Mfr Control No</i>	<i>Subject No</i>
18-Nov-05	0390		Protocol Amendment: New Investigator		SP756	New and revised investigators		
21-Nov-05			General Correspondence			Schwarz emails Ms. Melina Griffiths, FDA, regarding biowaiver for syrup.		
21-Nov-05			FDA Correspondence			Ms. Calder, FDA, emails that biowaiver is reasonable but bioequivalence study between the tablet and 10 mg/mL syrup study, SP657, is preliminary and subject to extensive review during NDA stage		
22-Nov-05	0391		Initial Safety Report		SP754		2005-00775	12512/80299
30-Nov-05	0392		Information Amendment: Clinical		SP690	An open-label follow-on trial to assess the long-term safety and efficacy of oral SPM 927 in subjects with postherpetic neuralgia (PHN)		
30-Nov-05	0392		Information Amendment: Clinical		SP611	An open-label trial to assess the efficacy and safety of ascending doses of SPM 927 in subjects with chronic refractory neuropathic pain		
02-Dec-05	0393		General Correspondence			Request finalized list of FDA attendees and anticipated date of preliminary response to questions submitted in pre-NDA meeting package (Serial No. 0325); submit list of Schwarz attendees		
05-Dec-05	0394		Follow-up Safety Report		SP768		2005-00096	112703/80093
07-Dec-05	0395		Initial Safety Report		SP774		2005-00803	110505/83749
08-Dec-05	0396		Follow-up Safety Report		SP863		2005-00662	80011/80011

Monday, November 10, 2008

IND 57,939

Page 87 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
13-Dec-05	0397		Response to FDA Request for Information		Submit information requested by Dr. Broadbent, FDA, for verification that both the masking agent and the strawberry flavoring are Generally Recognized as Safe (GRAS)		
14-Dec-05	0398		Follow-up Safety Report	SP768		2005-00552	102704
14-Dec-05	0398		Follow-up Safety Report	SP615		2005-00465	10477
15-Dec-05	0399		Initial Safety Report	SP830		2005-00821	110604
19-Dec-05	0400		Follow-up Safety Report	SP615		2005-00253	10476
19-Dec-05	0400		Follow-up Safety Report	SP768		2005-00060	111305/80162
20-Dec-05	0401		Initial Safety Report	SP745		2005-00827	108112
21-Dec-05	0402		Follow-up Safety Report	SP774		2005-00803	110505/83749
21-Dec-05	0403		Protocol Amendment: New Investigator	SP756		New and revised investigators	
21-Dec-05	0403		Protocol Amendment: New Investigator	SP615		Revised investigators	
27-Dec-05	0404		7-Day Safety Report	SP830		2005-00843	115201
03-Jan-06	0405		Initial Safety Report	SP745		2005-00848	109209
03-Jan-06	0405		Initial Safety Report	SP774		2005-00834	122105

Monday, November 10, 2008

IND 57,939

Page 88 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
09-Jan-06	0406		Follow-up Safety Report	SP830		2005-00821	110604
09-Jan-06	0407		Request FDA Comment	754, SP755, SP830	Submit proposed statistical analysis plan for protocol SP754 which may also apply to all double-blind trials in support of the treatment of epilepsy		
09-Jan-06	0408	v1	Information Amendment: Clinical	SP616	A multicenter, double-blind, double-dummy, randomized trial to investigate the safety, tolerability and pharmacokinetics of intravenous SPM 927 as replacement for oral SPM 927 in subjects with partial seizures with or without secondary generalization		
09-Jan-06	0408	v2	Information Amendment: Clinical	SP661	Randomized, double-blind, placebo-controlled, parallel-group, Phase 1 trial to evaluate the pharmacokinetics, safety, and tolerability following multiple-dose oral treatment of 200mg SPM 927 in healthy male White, Black, and Asian subjects		
09-Jan-06	0408	v2 p249	Information Amendment: Clinical	SP665	An open-label follow-on trial to assess the long-term safety and efficacy of oral SPM 927 in subjects with diabetic neuropathy		
13-Jan-06	0409		7-Day Safety Report	SP746		2005-00400	16304
16-Jan-06	0410		Follow-up Safety Report	SP745		2005-00827	108112
16-Jan-06	0410		Follow-up Safety Report	SP745		2005-00848	109209
16-Jan-06	0410		Follow-up Safety Report	SP640		2005-00636	82043

Monday, November 10, 2008

IND 57,939

Page 89 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
17-Jan-06			7-Day Safety Report Fax	SP745		2006-00017	104902
17-Jan-06			General Correspondence	SP768	Email Ms. Calder, Ms. Griffiths, and Ms. Malandra, FDA, notification that Schwarz will be submitting safety information		
17-Jan-06	0411		General Correspondence	SP768	Submit safety update		
17-Jan-06	0412		7-Day Safety Report	SP745		2005-00017	104902
18-Jan-06	0413		7-Day Safety Report	SP745		2006-00019	104910
20-Jan-06			General Correspondence	SP768	Email Ms. Malandro and Ms. Calder, FDA, outlier analysis for SP768 submitted 20-JAN-2006		
20-Jan-06			FDA Correspondence	SP768	Ms. Calder, FDA, confirms receipt of email containing outlier analysis for SP768		
20-Jan-06	0414		7-Day Safety Report	SP615		2005-00031	11522
20-Jan-06	0415		Protocol Amendment: New Investigator	SP756	New investigators		
20-Jan-06	0415		Protocol Amendment: New Investigator	SP754	Revised investigators		
20-Jan-06	0415		Protocol Amendment: New Investigator	SP615	Revised investigator		
20-Jan-06	0416		General Correspondence	SP768	Submit outlier analysis of SP768		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
23-Jan-06			FDA Correspondence	754, SP755, SP6	Ms. Calder, FDA, emails comment from statistical team regarding proposed statistical analysis plan submitted 9-JAN-2006		
23-Jan-06	0417		General Correspondence	SP768	Submit IDMC data for 24-JAN-2006 teleconference (rescheduled to 27-JAN-2006 at 1:30pm)		
24-Jan-06	0418		Follow-up Safety Report	SP754		2005-00370	12804/80207
24-Jan-06	0418		Follow-up Safety Report	SP774		2005-00834	122105
01-Feb-06	0419		Response to FDA Request for Information	SP746, SP830,	Submit minutes from IDMC closed session on 31-JAN-2006 and report how Schwarz is responding to IDMC's conclusions		
02-Feb-06			FDA Correspondence		Ms. Calder, FDA, emails that the Division may want to meet in the future but the medical team is still reviewing information submitted 1-FEB-2006		
02-Feb-06			General Correspondence		Email Ms. Calder, FDA, to ask if Division of Neurology Products is considering meeting over information provided 1-FEB-2006		
03-Feb-06			FDA Phone Contact		Ms. Calder, FDA, calls to notify of a 6-FEB-2006 teleconference from 3:00-4:00pm to discuss safety information for lacosamide including the data submitted 17-JAN-2006 and 1-FEB-2006		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
06-Feb-06			General Correspondence		Email Ms. Calder, FDA, to confirm 6-FEB-2006 teleconference and confirm conference call number and conference code		
06-Feb-06			SB Meeting Minutes		SB draft meeting minutes from 06-FEB-2006 teleconference		
07-Feb-06	0420		Follow-up Safety Report	SP745		2005-00631	111607
07-Feb-06	0420		Follow-up Safety Report	SP774		2005-00834	122105
08-Feb-06			FDA Correspondence		Ms. Calder, FDA, emails report of delayed email		
10-Feb-06	0421		Information Amendment: Clinical	SP660	Randomized, open-label, single- and multiple-dose trial to evaluate the pharmacokinetic effect as well as safety and tolerability of SPM 927 on metformin and vice versa in healthy male Caucasian subjects		
10-Feb-06	0421		Information Amendment: Clinical	SP598	An open-label extension study of the safety, tolerability, and compatibility of the continued administration of harkoseride (SPM 927, ADD 234037) as adjunctive therapy in patients with partial seizures		
10-Feb-06	0422		Initial Safety Report	SP774		2006-00074	2006-00074
10-Feb-06	0422		Initial Safety Report	SP746		2006-00056	14801

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
13-Feb-06	0423		Information Amendment: CMC Data		Submit revised CMC data which includes updated information on drug substance and drug product		
16-Feb-06	0424		Follow-up Safety Report	SP746		2005-00400	16304
16-Feb-06	0424		Follow-up Safety Report	SP774		2005-00834	122105
16-Feb-06	0424		Follow-up Safety Report	SP745		2006-00019	104910
17-Feb-06	0425		Request FDA Comment		Submit revised Informed Consent Form for review		
21-Feb-06	0426		Protocol Amendment: New Investigator	SP756	New investigator		
21-Feb-06	0426		Protocol Amendment: New Investigator	SP615	Revised investigators		
21-Feb-06	0426		Protocol Amendment: New Investigator	SP754	Revised investigator		
23-Feb-06	0427		Follow-up Safety Report	SP768		2005-00444	112305/80382
23-Feb-06	0427		Follow-up Safety Report	SP768		2005-00634	104610/80545
23-Feb-06	0427		Follow-up Safety Report	SP768		2005-00061	111307/80163
23-Feb-06	0427		Follow-up Safety Report	SP768		2005-00544	114721/80494
23-Feb-06	0427		Follow-up Safety Report	SP768		2005-00750	104214/80312

Monday, November 10, 2008

IND 57,939

Page 93 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
			<i>Type</i>	<i>Submision</i>			<i>Mfr Control No</i>	<i>Subject No</i>
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00744	108217/80452
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00096	112703/80093
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00643	109138/80573
23-Feb-06	0427		Follow-up Safety Report		SP768		2004-00790	112104/80001
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00556	106313/80468
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00552	102704/80359
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00545	108808/80185
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00533	103902/80631
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00089	112909/80024
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00424	101410/80256
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00358	108702/80471
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00119	110403/80108
23-Feb-06	0427		Follow-up Safety Report		SP768		2005-00375	109308/80117
27-Feb-06	0428		7-Day Safety Report		SP830		2005-00644	105616
28-Feb-06	0429		7-Day Safety Report		SP745		2006-00114	106316

Monday, November 10, 2008

IND 57,939

Page 94 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
<i>Date</i>	<i>No</i>	<i>Type</i>	<i>Location</i>			<i>Mfr Control No</i>		
01-Mar-06	0430	Follow-up Safety Report		SP745		2005-00597		111308
01-Mar-06	0430	Follow-up Safety Report		SP774		2006-00074		110405
01-Mar-06	0430	Follow-up Safety Report		SP774		2005-00803		110505/83749
03-Mar-06	0431	General Correspondence			Request FDA review and comment on revised IB and ICF			
07-Mar-06		General Correspondence			Email Ms. Calder, FDA, about status of review of the IB and ICF for Iacosamide			
08-Mar-06		FDA Correspondence			Ms. Calder, FDA, emails successful receipt of electronic copy of 03-MAR-2006 IB and ICF submission			
08-Mar-06		General Correspondence			Email Ms. Calder, FDA, submission details for 03-MAR-2006 IB and ICF submission			
08-Mar-06		FDA Correspondence			Ms. Calder, FDA, emails that the Division has not yet seen 03-MAR-2006 IB and ICF submission			
08-Mar-06		General Correspondence			CC Ms. Calder email copy of 03-MAR-2006 IB and ICF submission			
08-Mar-06		FDA Correspondence			Ms. Calder, FDA, emails that she did not receive electronic copy of 03-MAR-2006 IB and ICF submission			
08-Mar-06		General Correspondence			Email Ms. Calder, FDA, first half of 03-MAR-2006 IB and ICF submission			

Monday, November 10, 2008

IND 57,939

Page 95 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
08-Mar-06			General Correspondence		Email Ms. Calder, FDA, second half of 03-MAR-2006 IB and ICF submission		
13-Mar-06			General Correspondence		Email Ms. Calder, FDA, thanks for comments on ICF		
13-Mar-06			FDA Correspondence		Ms. Calder, FDA, emails comments on revised ICF and suggests added language		
15-Mar-06	0432		Follow-up Safety Report	SP746		2006-00056	14801
15-Mar-06	0432		Follow-up Safety Report	SP774		2005-00803	110505/83749
15-Mar-06	0433		Initial Safety Report	SP830		2006-00129	115104
20-Mar-06	0434		Protocol Amendment: New Investigator	SP754	Revised investigators		
20-Mar-06	0434		Protocol Amendment: New Investigator	SP756	New investigators		
21-Mar-06	0435		Follow-up Safety Report	SP830		2005-00644	105616
29-Mar-06	0436		Information Amendment: Pharmacology/Toxicology	LPT 78604/02	6-Week subchronic toxicity study of SPM 927 by oral administration to juvenile CD® rats - age at start of administration: 7 days		
30-Mar-06			General Correspondence		Email Ms. Calder, FDA, to ask if there is any update in the review of the IB		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
31-Mar-06			FDA Correspondence		Ms. Calder, FDA, emails that next week she will follow up with the medical officer reviewing the IB		
31-Mar-06			7-Day Safety Report Fax		Fax 31-Mar-2006 7-day safety report to Division		
31-Mar-06	0437		7-Day Safety Report	SP757		2006-00158	170106
05-Apr-06	0438		Follow-up Safety Report	SP755		2005-00405	110109/83605
05-Apr-06	0438		Follow-up Safety Report	SP755		2005-00008	122303/87995
05-Apr-06	0438		Follow-up Safety Report	SP755		2004-00785	11601/85761
05-Apr-06	0438		Follow-up Safety Report	SP755		2005-00077	108401/82989
05-Apr-06	0438		Follow-up Safety Report	SP755		2005-00602	124609/88827
05-Apr-06	0438		Follow-up Safety Report	SP755		2005-00206	108202/82918
05-Apr-06	0438		Follow-up Safety Report	SP755		2005-00323	106406/82273
06-Apr-06	0439		7-Day Safety Report	SP757		2006-00166	170111
06-Apr-06	0440		Initial Safety Report	SP774		2006-00161	108404/8292
13-Apr-06	0441		Initial Safety Report	SP830		2006-00163	101109
14-Apr-06	0442		Meeting Request		Request Type B Pre-NDA meeting with Division of Neurology Products		

Monday, November 10, 2008

IND 57,939

Page 97 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Apr-06	0443		Protocol Amendment: New Investigator	SP615	Revised investigators		
20-Apr-06	0443		Protocol Amendment: New Investigator	SP756	New investigators		
20-Apr-06	0444		Follow-up Safety Report	SP745		2006-00114	106316
20-Apr-06	0444		Follow-up Safety Report	SP757		2006-00158	170106
20-Apr-06	0444		Follow-up Safety Report	SP757		2006-00166	170111
21-Apr-06	0445		General Correspondence		Submit cardiovascular analysis, as requested in 6-FEB-2006 teleconference with the division		
24-Apr-06			FDA Correspondence	SP757	Ms. Calder, FDA, emails to report subject number for adverse event report referenced in same-day email	2006-00158	170106
24-Apr-06			FDA Correspondence	SP757	Ms. Calder, FDA, emails questions about adverse event report and asks that Schwarz examine possible causality to medication and adequacy of cardiac monitoring during infusion	2006-00158	170106
25-Apr-06	0446		General Correspondence	40724/1	Submit rationale and draft protocols for juvenile dog studies for FDA review and comment		
25-Apr-06	0446		General Correspondence	40724/2	Submit rationale and draft protocols for juvenile dog studies for FDA review and comment		

Monday, November 10, 2008

IND 57,939

Page 98 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
26-Apr-06			FDA Correspondence		Ms. Calder, FDA, emails to grant type B meeting 19-JULY-2006		
26-Apr-06	0447		Initial Safety Report	SP774		2006-00066	124406
27-Apr-06			General Correspondence		Email Ms. Calder, FDA, to question if 19-JULY-2006 meeting will be one hour, from 11:00-12:00pm		
27-Apr-06			FDA Correspondence		Ms. Calder, FDA, emails to offer option for 19-JULY-2006 meeting to last from 10:30-12:00pm		
27-Apr-06	0448		Initial Safety Report	SP745		2005-00598	172207
27-Apr-06	0449		Follow-up Safety Report	SP774		2006-00161	108404/8292
27-Apr-06	0449		Follow-up Safety Report	SP830		2006-00163	101109
28-Apr-06			General Correspondence	SP757	Email Ms. Calder, FDA, preliminary response to 24-APRIL-2006 email requesting additional safety information	2006-00158	170106
01-May-06	0450		General Correspondence	SP757	Submit requested safety information	2006-00158	170106
03-May-06			FDA Correspondence		Ms. Calder, FDA, emails additional request for suicidality data		
03-May-06	0451		Initial Safety Report	SP756		2006-00186	12202

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
05-May-06	0452		Information Amendment: Clinical	SP641	Open, non-randomized, sequential group comparison to investigate the pharmacokinetics, safety, and tolerability of 100mg SPM 927 in m&f subj. with renal impairment incl. subj. requiring dialysis compared with m&f healthy subj. following single-dose admin.		
11-May-06	0453		General Correspondence		Submit narratives for cardiovascular analysis		
12-May-06			General Correspondence		Email Ms. Calder, FDA, to request status of the review of draft protocols submitted 25-APR-2006		
15-May-06			FDA Correspondence		Ms. Calder, FDA, emails that toxicology reviewer will not review 25-APR-2006 draft protocols for a few weeks		
15-May-06			FDA Correspondence		Ms. Calder, FDA, emails that the reviewer of IB hopes to have comments within the week		
15-May-06			General Correspondence		Email Ms. Calder, FDA, to ask about status of draft toxicology studies		
15-May-06			FDA Correspondence		Ms. Calder, FDA, emails that the 25-APR-2006 draft protocols have not been reviewed yet but would be within the next week		
15-May-06			General Correspondence		Email Ms. Calder, FDA, to ask if a toxicologist will be reviewing 25-APR-2006 draft protocols		

Monday, November 10, 2008

IND 57,939

Page 100 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
15-May-06			General Correspondence		Email Ms. Calder, FDA, thanks for information on review timeline for 25-APR-2006 draft toxicology protocol submission		
18-May-06	0454		Initial Safety Report	SP774		2006-00032	110406
18-May-06	0454		Initial Safety Report	SP754		2006-00209	14312/80405
19-May-06	0455		Protocol Amendment: New Investigator	SP615	Revised investigators		
19-May-06	0455		Protocol Amendment: New Investigator	SP756	New investigators		
22-May-06	0456		Follow-up Safety Report	SP745		2005-00598	172207
22-May-06	0456		Follow-up Safety Report	SP754		2005-00775	12512/80299
22-May-06	0456		Follow-up Safety Report	SP830		2006-00129	115104
22-May-06	0456		Follow-up Safety Report	SP830		2005-00644	105616
26-May-06	0457		Information Amendment: Clinical	SP743	A multi-center, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of 400mg/day and 600mg/day SPM 927 in subjects with painful distal diabetic neuropathy		
26-May-06	0457		Information Amendment: Clinical	SP742	A multi-center, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of 200, 400, and 600mg/day SPM 927 in subjects with painful distal neuropathy		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
30-May-06	0458		Protocol Amendment: Change in Protocol	SP754	Amendment 2		
30-May-06	0458		Protocol Amendment: Change in Protocol	SP615	Amendment 8		
30-May-06	0458		Protocol Amendment: Change in Protocol	SP756	Amendment 2		
01-Jun-06	0459		Follow-up Safety Report	SP830		2006-00129	115104
01-Jun-06	0459		Follow-up Safety Report	SP774		2006-00032	110406
02-Jun-06	0460		General Correspondence	SP755	Schwarz submits additional information requested by Calder, FDA, on 24-Apr-2006. Send revised narrative, cardiology consult reports and ECG reports	2006-00158	170106
07-Jun-06			General Correspondence		Email Ms. Calder, FDA, to request status of the review of Investigator's Brochure		
08-Jun-06			FDA Correspondence		Ms. Calder, FDA, emails that review of Investigator's Brochure is not completed but should be soon		
16-Jun-06	0461		Meeting Package		Submit meeting package for 19-JUL-2006 Pre-NDA Meeting		
20-Jun-06	0462		Protocol Amendment: New Investigator	SP756	New and revised investigators		
20-Jun-06	0462		Protocol Amendment: New Investigator	SP754	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 102 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Jun-06	0462		Protocol Amendment: New Investigator	SP615	Revised investigator		
23-Jun-06	0463		Annual Report		Period covering March 26, 2005 through March 25, 2006		
06-Jul-06			General Correspondence		Email Ms. Calder, FDA, to inquire about review of the IB		
06-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails okay to go ahead with implementation of the IB changes based on the reviewer's initial cursory look; he may have additional comments in the future		
12-Jul-06	0464		Follow-up Safety Report	SP830		2006-00129	115104
17-Jul-06			FDA Meeting Minutes		Pre-NDA pre-meeting minutes		
17-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails pre-NDA premeeting minutes and Clinical and Pharmacology Biopharmaceutics Review Aid		
17-Jul-06			General Correspondence		Email Ms. Calder, FDA, list of Schwarz attendees to pre-NDA meeting		
17-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails thanks for list of pre-NDA meeting attendees and reports that no hard copy is necessary		
17-Jul-06			General Correspondence		Email Ms. Calder, FDA, thanks for pre-NDA documents		

Monday, November 10, 2008

IND 57,939

Page 103 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
17-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails to ask for list of attendees to give to the guards		
18-Jul-06			General Correspondence		Email Ms. Calder, FDA, to confirm pre-NDA meeting 19-JUL-2006 from 10:30-12:00; also ask if titles of attendees are needed		
18-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails that attendee titles will be helpful to have		
18-Jul-06	0465		7-Day Safety Report	SP745		2006-00284	172723
18-Jul-06	0465		7-Day Safety Report	SP745		2006-00283	172719
20-Jul-06	0466		Protocol Amendment: New Investigator	SP615	Revised investigators		
20-Jul-06	0466		Protocol Amendment: New Investigator	SP754	Revised investigators		
20-Jul-06	0466		Protocol Amendment: New Investigator	SP756	New investigator		
21-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails to request slides presented in 19-JUL-2006 pre-NDA meeting		
21-Jul-06			General Correspondence		Email Ms. Calder, FDA, slide from 19-JUL-2006 pre-NDA meeting		
24-Jul-06			General Correspondence		Email Ms. Calder, FDA, list of Schwarz attendees to 19-JUL-2006 pre-NDA meeting and request list of FDA attendees		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
24-Jul-06			FDA Correspondence		Ms. Calder, FDA, emails list of FDA attendees to 19-JUL-2006 pre-NDA meeting		
25-Jul-06	0467		7-Day Safety Report	SP745		2006-00289	108305
31-Jul-06	0468		SB Meeting Minutes		Submit Pre-NDA Meeting Minutes from meeting held 19-JULY-2006		
02-Aug-06			General Correspondence		Mail to Dr. Levin, FDA, Type C meeting request with DNP, DAARP, and Office of Information Management to reach consensus with regard to technical aspects of filing lacosamide NDA		
02-Aug-06	0469		General Correspondence		Submit Type C meeting request with DNP, DAARP, and Office of Information Management to reach consensus with regard to technical aspects of filing lacosamide NDA		
07-Aug-06			FDA Phone Contact		Ms. Calder, FDA, calls to schedule a teleconference regarding abuse liability on 14-AUG-2006 from 10:30-11:00.		
07-Aug-06	0470		Initial Safety Report	SP830		2006-00293	10118
07-Aug-06	0470		Initial Safety Report	SP756		2006-00295	18906
08-Aug-06			FDA Meeting Minutes		Ms. Calder, FDA, emails minutes from Pre-NDA meeting held 19-JUL-2006		
09-Aug-06			FDA Correspondence		Ms. Calder, FDA, emails that the teleconference will need to be moved to 01-SEP-2006 from 12-12:30		

Monday, November 10, 2008

IND 57,939

Page 105 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
						<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
09-Aug-06			General Correspondence		Email Ms. Calder, FDA, that rescheduled 01-SEP-2006 teleconference date will be fine		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	10263	In vitro pharmacology – receptor binding assay with SPM 927 and SPM 12809		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	A22173	SPM 927: Ready biodegradability in a CO2 evolution (modified Sturm) test		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	A27033	SPM 927: Toxicity to activated sludge in a respiration inhibition test		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	E-006-05-04	Electrophysiological effects of SPM 12809 on the current mediated by the SCN5A-sodium channel stably expressed in CHO-K1 cells		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	RS211	Assessment of the dependence potential of SPM 927 in rats and dogs after chronic administration and abrupt withdrawal		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	05.122/6	Evaluation of SPM 927 in the conditioned place preference test in the rat		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	JRO 217.27.275.	Neuroprotective effect of SPM 927 on traumatic brain injury in rat		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	03.488/5	Evaluation of lacosamide, lamotrigine, levetiracetam, pregabalin, amitriptyline and venlafaxine in a model of neuropathic pain (Chung) in the rat (i.p. administration)		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	AA24877	Effects of SPM 927 (0.3, 1 and 3 mg/kg) on harmaline-induced tremors in rats		

Monday, November 10, 2008

IND 57,939

Page 106 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	F104017	Assessment of SPM 927 in the SOD1 transgenic mouse model of ALS		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	732	Determination of the cytochrome P450 induction potential of lacosamide in human hepatocytes		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	F9664	Effects of SPM 927 (harkoseride) on the development of amygdala kindling in rats		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	LPT 18601/04	6-week dose-range-finding study for a 6-week subchronic toxicity study of SPM 927 by oral administration to juvenile CD® rats – age at start of administration: 7 days		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	LPT 18602/04	6-week subchronic toxicity study of SPM 927 by oral administration to juvenile CD® rats – age at start of administration: 7 days		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	A22206	Adsorption/desorption of [14C]-SPM 927 on soils		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	F9696	Evaluation of SPM 927 and SPM 14221 in an animal model of fibromyalgia		
10-Aug-06	0471		Information Amendment: Pharmacology/Toxicology	A22184	SPM 927: Toxicity to scenedesmus subspicatus in a 72-hour algal growth inhibition test		
10-Aug-06	0472		Follow-up Safety Report	SP745		2005-00597	111308
16-Aug-06	0473		Follow-up Safety Report	SP774		2006-00161	108406/8292

Monday, November 10, 2008

IND 57,939

Page 107 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
17-Aug-06			FDA Correspondence		Ms. Calder, FDA, emails to grant 02-AUG-2006 request for a face-to-face type C meeting, to be held 06-SEP-06 from 3:30-4:30		
18-Aug-06			General Correspondence		Email Ms. Calder, FDA, to confirm if there will be a representative from DAARP and Randy Levin's group at 06-SEP-06 meeting		
21-Aug-06			FDA Correspondence		Ms. Calder, FDA, emails that Lisa Malandro from DAARP and Ken Edmonds will attend 06-SEP-2006 meeting		
21-Aug-06	0474		Protocol Amendment: New Investigator	SP615	Revised investigators		
21-Aug-06	0474		Protocol Amendment: New Investigator	SP756	Revised investigators		
22-Aug-06	0475		7-Day Safety Report	SP830		2006-00278	112204
24-Aug-06	0476		Follow-up Safety Report	SP756		2006-00295	18906
24-Aug-06	0476		Follow-up Safety Report	SP745		2006-00289	108305
25-Aug-06	0477		Information Amendment: Clinical	SP643	Randomized, open-label, two-way crossover trial to investigate the pharmacokinetics and bioavailability of SPM 927 in poor and extensive metabolizers (CYP 2C19)		

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS</i>
<i>Date</i>	<i>No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr</i>	<i>Control No</i>	<i>Subject No</i>
25-Aug-06	0477		Information Amendment: Clinical	SP644	Double-blind, placebo-controlled, randomized crossover Phase I trial to investigate a possible influence of SPM 927 on the steady state pharmacokinetics, pharmacodynamics, safety and tolerability of digoxin in healthy male Caucasian subjects			
25-Aug-06	0477		Information Amendment: Clinical	SP657	Randomized, open, 2-period crossover trial to show bioequivalence following single oral dosing of a tablet and of a liquid of 200mg SPM 927 each in healthy subjects			
25-Aug-06	0477		Information Amendment: Clinical	SP658	Randomized, open-label, single-dose, 3-way crossover trial to compare the pharmacokinetics of SPM 927 when given as intravenous solution or as oral tablet in 24 healthy male subjects			
25-Aug-06	0477		Information Amendment: Clinical	SP863	Open-label multiple-dose trial to evaluate the pharmacokinetic effect of lacosamide on omeprazole and vice versa in healthy male White subjects			
25-Aug-06	0477		Information Amendment: Clinical	SP599	A study of the potential pharmacodynamic and pharmacokinetic interaction of SPM 927 (harkoseride) with Microgyn® in healthy female subjects			
28-Aug-06	0478		Request FDA Comment	SP903	Request comment on abuse liability plan			
01-Sep-06			SB Meeting Minutes		Contact report summarizing 01-SEP-2006 teleconference with Neurology Products to discuss abuse liability			
01-Sep-06	0479		7-Day Safety Report	SP745			2006-00350	101802

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
01-Sep-06	0479		7-Day Safety Report	SP745		2006-00357	175702
01-Sep-06	0480		Information Amendment: Clinical		Submit Investigator's Brochure dated 29-AUG-2006		
06-Sep-06			SB Meeting Minutes		Schwarz internal summary of 06-OCT-2006 meeting with the FDA to discuss lacosamide electronic submission issues		
07-Sep-06	0481		Follow-up Safety Report	SP774		2006-00161	108406/8292
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	LPT 17963/04	Acute toxicity study of SPM 927 by single intravenous administration to CD-1 mice		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	04.270/3	Evaluation of SPM 927 in the behavioral despair test in the rat (i.p. administration)		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	6842-103	Rising dose tolerance oral (capsule) toxicity study of ADD 234037 in dogs		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	AA20234	Effects of SPM 927 on harmaline-induced tremors in rats		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	00704	Therapeutic effect of SPM 927 in painful osteoarthritis in the rat		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	00649	Effect of SPM 927 in ddC-induced painful neuropathy in the rat		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	00580	Therapeutic effect of test compounds in painful diabetic neuropathy in the rat		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	00575	Effect of SPM 927 in vincristine-induced painful neuropathy in the rat		

Monday, November 10, 2008

IND 57,939

Page 110 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	Olney	Evaluation of the potential of SPM 927 to induce acute neurotoxic changes in the adult rat brain		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	505	Effect of SPM 927 in an animal model for mania		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	S03311	An efficacy study of SPM 927 in a rat mammary tumor-induced bone pain model		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	04.064/3	Evaluation of SPM 927 in a model of visceral pain in the rat		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	SCHW 002	Evaluation of SPM 927 in an animal model for anxiety: stress-induced hyperthermia		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	SCHW001	Evaluation of SPM 927 alone and in combination with clozapine on the prepulse inhibition of the startle response in C56/BL6 mice		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	AA19072	Effects of SPM 927 on reserpine-induced tardive dyskinesia in mice		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	Krishtal	Electrophysiological characterization of SPM-927		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	8540	In vitro pharmacology: GABA transaminase assay		
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	507/511	Effect of SPM 927 in two animal models of anxiety		

Monday, November 10, 2008

IND 57,939

Page 111 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>		<i>Title/ Description</i>		<i>CIOMS</i>	<i>CIOMS</i>
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>					<i>Mfr Control No</i>	<i>Subject No</i>
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	LPT 17964/04		Acute toxicity study of SPM 927 by single oral administration to CD rats			
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	LPT 17962/04		28-Day immunotoxicological study of SPM 927 by repeated oral administration to CD-1 mice – plaque forming colony (PFC) test			
12-Sep-06	0482		Information Amendment: Pharmacology/Toxicology	Marzin-Lille		Expert report on the mutagenicity of SPM 927			
15-Sep-06	0483		Initial Safety Report	SP774				2006-00366	104504
15-Sep-06	0484		Follow-up Safety Report	SP830				2006-00278	112204
15-Sep-06	0484		Follow-up Safety Report	SP745				2006-00357	175702
18-Sep-06			General Correspondence	SP903		Email Ms. Calder, FDA, to request she follow up with CSS about timeline for response to 28-AUG-2006 abuse liability protocol submission			
19-Sep-06			General Correspondence	SP903		Email Ms. Calder, FDA, thanks for following up with CSS on abuse liability protocol review			
19-Sep-06			FDA Correspondence	SP903		Ms. Calder, FDA, emails that CSS has completed its review of the abuse liability protocol and will send comments soon			
20-Sep-06			General Correspondence			Email Ms. Calder, FDA, for feedback on questions in cover letter of abuse liability submission			

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
			<i>Type</i>	<i>Sub Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>	
20-Sep-06			FDA Correspondence		SP903	Ms. Calder, FDA, emails 'you're welcome' for recommendations regarding the abuse liability protocol			
20-Sep-06			FDA Correspondence		SP903	Ms. Calder, FDA, emails recommendations regarding the abuse liability protocol			
20-Sep-06			General Correspondence		SP903	Email Ms. Calder, FDA, thanks for recommendations regarding the abuse liability protocol			
20-Sep-06	0485		Protocol Amendment: New Investigator		SP754	Revised investigators			
20-Sep-06	0485		Protocol Amendment: New Investigator		SP756	Revised investigators			
26-Sep-06	0486		7-Day Safety Report		SP745		2006-00389		170304
02-Oct-06	0487		Meeting Request			Request type A meeting to discuss conversion from adjunctive treatment to monotherapy			
03-Oct-06			FDA Meeting Minutes			Ms. Calder, FDA, emails meeting minutes from 06-SEP-2006 meeting to discuss the electronic submission of multiple NDAs with multiple indications			
05-Oct-06			FDA Correspondence			Ms. Calder, FDA, emails to grant type A meeting 15-NOV-2006 from 3:00 - 4:00			
10-Oct-06	0488		Follow-up Safety Report		SP745		2006-00389		170304
16-Oct-06	0489		Initial Safety Report		SP874		2006-00403		125009/80029

Monday, November 10, 2008

IND 57,939

Page 113 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
16-Oct-06	0490		7-Day Safety Report	SP745		2005-00509	171324
19-Oct-06	0491		Initial Safety Report	SP774		2006-00409	122402
19-Oct-06	0492		Follow-up Safety Report	SP754		2005-00370	12804/80207
23-Oct-06	0493		7-Day Safety Report	SP830		2006-00420	105309
23-Oct-06	0494		General Correspondence	SP903	Submit Protocol SP903 integrating comments from CSS		
24-Oct-06	0495		Meeting Package	SP902	Submit Type A meeting package for 15-NOV-2006 meeting to discuss proof of concept protocol SP902		
25-Oct-06	0496		7-Day Safety Report	SP874		2006-00418	124701/80223
26-Oct-06	0497		Follow-up Safety Report	SP745		2006-00350	101802
26-Oct-06	0498		Information Amendment: Clinical	SP755	A multicenter, double-blind, randomized, placebo-controlled, parallel-group trial to investigate the efficacy and safety of SPM 927 (200 and 400mg/day) as adjunctive therapy in subjects with partial seizures with or without secondary generalization		
02-Nov-06	0499		Initial Safety Report	SP774		2006-00094	114109
02-Nov-06	0500		Follow-up Safety Report	SP774		2006-00409	122402
02-Nov-06	0500		Follow-up Safety Report	SP754		2006-00209	14312/80405

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
07-Nov-06	0501		Follow-up Safety Report	SP830		2006-00420	105309
09-Nov-06	0502		Follow-up Safety Report	SP830		2006-00278	112204
10-Nov-06			General Correspondence		Email Ms. Calder, FDA, list of Schwarz attendees for 15-NOV-2006 pre-NDA meeting		
13-Nov-06			FDA Correspondence		Ms. Calder, FDA, emails list of FDA attendees for 15-NOV-2006 pre-NDA meeting		
13-Nov-06	0503		Follow-up Safety Report	SP874		2006-00418	124701/80223
13-Nov-06	0503		Follow-up Safety Report	SP830		2006-00129	115104
14-Nov-06			FDA Meeting Minutes		Ms. Calder, FDA, emails pre-meeting minutes for 15-NOV-2006 pre-NDA meeting		
15-Nov-06	0504		Follow-up Safety Report	SP830		2006-00438	105318
20-Nov-06	0505		Protocol Amendment: New Investigator	SP615	Revised investigator		
20-Nov-06	0505		Protocol Amendment: New Investigator	SP754	Revised investigator		
28-Nov-06	0506		Follow-up Safety Report	SP830		2006-00438	105318
28-Nov-06	0506		Follow-up Safety Report	SP874		2006-00418	124701/80223

Monday, November 10, 2008

IND 57,939

Page 115 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
28-Nov-06	0506		Follow-up Safety Report	SP874		2006-00403	125009/80029
04-Dec-06			FDA Meeting Minutes	SP902	Ms. Calder, FDA, emails meeting minutes from 15-NOV-2006 meeting on monotherapy		
05-Dec-06			SB Meeting Minutes	SP902	Email Ms. Calder, FDA, Schwarz minutes from 15-NOV-2006 meeting on monotherapy		
05-Dec-06	0507		7-Day Safety Report	SP874		2006-00472	102205/80148
05-Dec-06	0508		SB Meeting Minutes		Submit minutes from 15-NOV-2006 Type A meeting		
06-Dec-06	0509		General Correspondence		Submit IDMC correspondence wherein IDMC informs Schwarz that lacosamide up to 600mg can be allowed in trials of subjects with diabetic peripheral neuropathy		
11-Dec-06	0510		7-Day Safety Report	SP874		2006-00478	129704/80308
19-Dec-06	0511		Protocol Amendment: New Investigator	SP756	Revised investigator		
19-Dec-06	0512		Initial Safety Report	SP830		2006-00495	114006
19-Dec-06	0513		Follow-up Safety Report	SP874		2006-00478	129704/80308
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	699/46	A study of absorption, distribution, metabolism and excretion following oral administration to the mouse		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	826	SPM 927: Metabolite profiling and identification in the mouse, rat and dog		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	865	Inhibition of the cytochrome P450 isoenzymes 1A1, 2A6, 2B6, 2C8, 2E1 and 3A5 by SPM 927 and SPM 12809		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	847	Structure proposal for polar metabolite		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	A45180	SPM 927: Toxic effects to zebra fish (Brachydanio rerio) in an early-life stage toxicity test		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	Drommer	SPM 927 Light and electron microscopical investigation of liver tissues from study "13-week oral gavage subchronic toxicity of ADD 234037 in rats"		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	A45202	SPM 927: Effect on survival and reproduction of Daphnia magna in a semi-static test over three weeks		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	8540	In Vitro Pharmacology: GABA Transaminase Assay – Study of SPM 927		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	699/47	SPM 927: A study of absorption and excretion following oral administration to the rat		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	699/48	A study of absorption, distribution, metabolism and excretion following oral and intravenous administration to the dog		

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	699/17	(14C)-SPM 927: Quantitative whole-body autoradiography following oral and intravenous administration to the pigmented rat		
20-Dec-06	0514		Information Amendment: Pharmacology/Toxicology	F9672	Evaluation of the neuroprotective efficacy of compound SPM 927 in rat hippocampal slice cultures after OGD, glutamate and staurosporine insult		
21-Dec-06	0515		Initial Safety Report	SP774		2006-00481	112315
22-Dec-06	0516		Initial Safety Report	SP874		2006-00488	115902/80260
22-Dec-06	0517		Follow-up Safety Report	SP874		2006-00472	102205/80148
03-Jan-07	0518		Initial Safety Report	SP745		2006-00510	110718
03-Jan-07	0518		Initial Safety Report	SP615		2006-00515	10191
03-Jan-07	0519		Follow-up Safety Report	SP745		2006-00289	108305
03-Jan-07	0520		7-Day Safety Report	SP756		2006-00473	15606
17-Jan-07	0521		Initial Safety Report	SP774		2007-00013	116206
17-Jan-07	0522		Follow-up Safety Report	SP830		2006-00495	114006
17-Jan-07	0522		Follow-up Safety Report	SP874		2006-00488	115902/80260
17-Jan-07	0523		7-Day Safety Report	SP874		2007-00020	129506/80472

Monday, November 10, 2008

IND 57,939

Page 118 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS</i>
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>Subject No</i>	
17-Jan-07	0523		7-Day Safety Report	SP874		2007-00023	115702/80415	
19-Jan-07	0524		Protocol Amendment: New Investigator	SP756	Revised Investigator			
24-Jan-07	0525		Information Amendment: Pharmacology/Toxicology	031209	Identification of harkoseride (SPM 927) targets using affinity capture and proteomics technologies			
24-Jan-07	0525		Information Amendment: Clinical	SP757	A multicenter, open-label trial to investigate the safety and tolerability of intravenous SPM 927 as replacement for oral SPM 927 in subjects with partial seizures with or without secondary generalization			
30-Jan-07	0526		Follow-up Safety Report	SP874		2007-00023	115702/80415	
30-Jan-07	0526		Follow-up Safety Report	SP745		2006-00510	110718	
30-Jan-07	0527		7-Day Safety Report	SP874		2006-00464	126603/80275	
31-Jan-07			FDA Correspondence		Ms. Calder, FDA, emails that CSS says Schwarz adequately responded to comments conveyed in NOV-2006 and CSS has no additional comments about protocol			
08-Feb-07	0528		Initial Safety Report	SP774		2007-00029	116205	
12-Feb-07	0529		7-Day Safety Report	SP745		2007-00055	175516	
12-Feb-07	0529		7-Day Safety Report	SP745		2007-00048	100806	

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
12-Feb-07	0530		Follow-up Safety Report	SP615		2006-00515	2006-00515
12-Feb-07	0530		Follow-up Safety Report	SP874		2006-00464	126603/80275
20-Feb-07	0531		Protocol Amendment: New Investigator	SP615	Revised investigators		
20-Feb-07	0531		Protocol Amendment: New Investigator	SP756	Revised investigator		
20-Feb-07	0532		7-Day Safety Report	SP746		2007-00068	102802
20-Feb-07	0533		Initial Safety Report	SP746		2007-00066	125012
20-Feb-07	0533		Initial Safety Report	SP745		2007-00061	108703
20-Feb-07	0534		Follow-up Safety Report	SP874		2007-00020	129506/80472
23-Feb-07	0535		7-Day Safety Report	SP830		2007-00074	116001
23-Feb-07	0535		7-Day Safety Report	SP746		2007-00056	110804/80106
23-Feb-07	0535		7-Day Safety Report	SP745		2007-00076	170801
23-Feb-07	0536		Follow-up Safety Report	SP874		2006-00464	126603/80275
27-Feb-07	0537		Follow-up Safety Report	SP615		2003-00367	11776
27-Feb-07	0537		Follow-up Safety Report	SP746		2007-00068	102802

Monday, November 10, 2008

IND 57,939

Page 120 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
05-Mar-07	0538		Follow-up Safety Report	SP830		2007-00074	116001
12-Mar-07	0539		7-Day Safety Report	SP874		2007-00088	121012/80641
14-Mar-07	0540		Information Amendment: Clinical	SP640	A double-blind, single-site, randomized, placebo- and positive-controlled, parallel-design trial of the electrocardiographic effects of 400 and 800mg per day of lacosamide in healthy male and female subjects: a thorough QT trial		
15-Mar-07			FDA Correspondence	SP902	Ms. Calder, FDA, emails acknowledgement of teleconference request		
15-Mar-07			General Correspondence	SP902	Email Ms. Calder, FDA, to request a monotherapy teleconference to discuss an additional statistical questions		
15-Mar-07	0541		Meeting Request	SP902	Request follow-up teleconference to discuss conversion from adjunctive treatment to monotherapy		
19-Mar-07	0542		General Correspondence		Request comment on plan to submit integrated safety datasets for all patients in phase 2b/3 trials		
20-Mar-07	0543		Initial Safety Report	SP774		2006-00319	124611
20-Mar-07	0544		Follow-up Safety Report	SP874		2006-00488	115902/80260
20-Mar-07	0544		Follow-up Safety Report	SP830		2006-00420	105309

Monday, November 10, 2008

IND 57,939

Page 121 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Mar-07	0545		Protocol Amendment: New Investigator	SP615	Revised investigators		
23-Mar-07	0546		General Correspondence	SP906	Updated cardiovascular safety report		
26-Mar-07			General Correspondence	SP902	Email Ms. Calder, FDA, follow-up to request for teleconference		
26-Mar-07			FDA Correspondence	SP902	Ms. Calder, FDA, emails that they will respond in writing to teleconference request		
26-Mar-07	0547		7-Day Safety Report	SP874		2007-00100	101408/80363
26-Mar-07	0548		Follow-up Safety Report	SP746		2007-00066	125012
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	Morrow	Harkosride in pre-clinical animal models of pain		
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	C13703	The effects of lacosamide in an animal model for migraine		
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	05.237/5	Evaluation of SPM 927 as a discriminative stimulus in a drug discrimination procedure in the rat		
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	05.673/4	Evaluation of SPM 927 for abuse potential using an i.v. self-administration paradigm in the rat		
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	05.264/2	Pseudo-isobolographic evaluation in combination with 5 other analgesic substances using the formalin (late phase) test in the rat (i.p. administration)		

Monday, November 10, 2008

IND 57,939

Page 122 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>CIOMS</i>		<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>Mfr Control No</i>	<i>Subject No</i>
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	'B-PDG-2006-521	UVVIS-absorption of O-desmethyl-lacosamide (SPM 12809)		
04-Apr-07	0549		Information Amendment: Pharmacology/Toxicology	IS-4-2311 Adden	Addendum to the study report: the early evaluation of anticonvulsant drugs		
11-Apr-07			General Correspondence	SP902	Email Ms. Calder, FDA, request for comments before Schwarz submits protocol SP902		
12-Apr-07			FDA Correspondence	SP902	Ms. Calder, FDA, emails comment on calculation of primary endpoint and says protocol can be submitted		
13-Apr-07	0550		Follow-up Safety Report	SP874		2007-00088	121012/80641
13-Apr-07	0550		Follow-up Safety Report	SP745		2007-00061	108703
16-Apr-07			FDA Correspondence	SP902	Ms. Calder, FDA, emails that submitting protocol SP902 as an SPA is not a good idea		
16-Apr-07			General Correspondence	SP902	Email Ms. Calder, FDA, additional question about submission of protocol SP902 as an SPA		
17-Apr-07	0551		Response to FDA Request for Information	SP640	Submit SP640 data in response to 22-MARCH-2007 email request from Malandro		
18-Apr-07			FDA Correspondence	SP902	Ms. Calder, FDA, emails additional comment about dropout criteria		
20-Apr-07	0552		Protocol Amendment: New Investigator	SP615	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 123 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Apr-07	0552		Protocol Amendment: New Investigator	SP754	Revised investigators		
23-Apr-07			7-Day Safety Report Fax	SP745		2005-00835	174203
23-Apr-07	0553		7-Day Safety Report	SP745		2005-00835	174203
23-Apr-07	0554		Initial Safety Report	SP756		2006-00422	17407
23-Apr-07	0555		Follow-up Safety Report	SP615		2003-00367	11776
24-Apr-07	0556		Information Amendment: Clinical	SP754	A multicenter, double-blind, randomized, placebo-controlled, parallel-group trial to investigate the efficacy and safety of SPM 927 (400 and 600 mg/day) as adjunctive therapy in subjects with partial seizures with or without secondary generalization		
27-Apr-07			Safety Report Fax	SP830		2006-00098	115110
27-Apr-07	0557		Protocol Amendment: New Protocol	SP904			
27-Apr-07	0557		Protocol Amendment: New Protocol	SP902			
27-Apr-07	0558		7-Day Safety Report	SP830		2006-00098	115110
03-May-07	0559		Follow-up Safety Report	SP874		2007-00100	101408/80363
09-May-07	0560		Initial Safety Report	SP756		2007-00140	14308

Monday, November 10, 2008

IND 57,939

Page 124 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>		<i>CIOMS Subject No</i>
			<i>Type</i>	<i>Submission</i>			<i>Mfr Control No</i>	<i>Subject No</i>	
09-May-07	0561		Follow-up Safety Report		SP830		2006-00098		115110
09-May-07	0561		Follow-up Safety Report		SP745		2006-00510		110718
09-May-07	0562		Information Amendment: Pharmacology/Toxicology		977	Metabolite turnover of SPM 927, SPM 6912 and SPM 12809 in S9 fractions obtained from male rat and human livers			
09-May-07	0562		Information Amendment: Pharmacology/Toxicology		1000	Profiling of polar metabolite			
16-May-07	0563		Request FDA Comment		raft, LPT 20614/1	Request for FDA review and comment and teleconference to discuss Division's response			
17-May-07	0564		General Correspondence		SP754, SP756	Submit follow up information in response to 04-MAY-2007 email from Lana Chen, FDA	000#5#2006-00422		17407
18-May-07	0565		Protocol Amendment: New Investigator		SP615	Revised investigators			
18-May-07	0565		Protocol Amendment: New Investigator		SP756	Revised investigators			
21-May-07			7-Day Safety Report Fax		SP745		2005-00463		176213
21-May-07	0566		7-Day Safety Report		SP745		2005-00463		176213
21-May-07	0567		Follow-up Safety Report		SP745		2006-00510		110718
22-May-07	0568		Follow-up Safety Report		SP756		2006-00442		17407

Monday, November 10, 2008

IND 57,939

Page 125 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
23-May-07			FDA Correspondence		Ms. Griffis, FDA, emails request for ClinPharm information, transmittal of ECGs to ECG warehouse, and copy of current IB		
07-Jun-07	0569		7-Day Safety Report	SP745		2007-00155	109133
08-Jun-07			General Correspondence		Email Ms. Griffis, FDA, completed ClinPharm table and latest IB in response to 23-MAY-2007 email request and ask about trade name review		
08-Jun-07			FDA Correspondence		Ms. Griffis, FDA, emails additional questions from QT group and response to DMETs trade name question		
14-Jun-07			General Correspondence		Email Ms. Griffis, FDA, documents regarding the appearance of tablets as requested in 08-JUN-2007 email		
14-Jun-07	0570		Information Amendment: CMC Data				
20-Jun-07	0571		Protocol Amendment: New Investigator	SP615	Revised investigator		
20-Jun-07	0571		Protocol Amendment: New Investigator	SP756	Revised investigators		
21-Jun-07			General Correspondence		Email Ms. Griffis, FDA, plan to submit one all-inclusive NDA under one NDA number		
22-Jun-07	0572		Initial Safety Report	SP874		2007-00119	124413/80424

Monday, November 10, 2008

IND 57,939

Page 126 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
25-Jun-07	0573		Annual Report		For the period 26-MAR-2006 through 25-MAR-2007		
27-Jun-07	0574		Information Amendment: Clinical	SP746 subtrial	A double-blind, randomized withdrawal of lacosamide in subjects with painful diabetic neuropathy - subtrial to SP746		
06-Jul-07	0575		7-Day Safety Report	SP746		2007-00199	124902
06-Jul-07	0576		Initial Safety Report	SP774		2007-00201	106404
06-Jul-07	0577		General Correspondence		Rquest for trade name review for Vimpat, Vondario, and Elzacra		
12-Jul-07	0578		Initial Safety Report	SP746		2007-00203	101208
13-Jul-07			FDA Phone Contact		Discuss proposed schematic of NDA/eCTD organization and obtain updated status of juvenile toxicology protocol review		
19-Jul-07	0579		7-Day Safety Report	SP746		2007-00214	105622
20-Jul-07	0580		Protocol Amendment: New Investigator	SP904	New investigators		
20-Jul-07	0580		Protocol Amendment: New Investigator	SP902	New investigators		
20-Jul-07	0580		Protocol Amendment: New Investigator	SP756	New investigator		

Monday, November 10, 2008

IND 57,939

Page 127 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Jul-07	0581		Response to FDA Request for Information		Submit additional information request by Ms. Griffis regarding proposed trade name submission		
23-Jul-07			FDA Correspondence		Ms. Griffis, FDA, emails comments from nonclinical team regarding draft protocol for juvenile dog toxicity study		
23-Jul-07			FDA Phone Contact		Ms. Griffis, FDA, called on behalf of DMETS to request additional information on trade name review submission		
30-Jul-07	0582		7-Day Safety Report	SP830		2007-00230	105806
30-Jul-07	0583		Follow-up Safety Report	SP745		2005-00835	174203
06-Aug-07	0584		Follow-up Safety Report	SP830		2007-00074	116001
08-Aug-07	0585		Initial Safety Report	SP746		2007-00231	118301
14-Aug-07	0586		7-Day Safety Report	SP615		2005-00465	10477
15-Aug-07	0587		7-Day Safety Report	SP830		2007-00248	114211
15-Aug-07	0587		7-Day Safety Report	SP745		2007-00246	110907
15-Aug-07	0587		7-Day Safety Report	SP746		2007-00244	102717
20-Aug-07	0588		7-Day Safety Report	SP830		2005-00618	105019
20-Aug-07	0589		Protocol Amendment: New Investigator	SP756	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 128 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Type</i>	<i>Location</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Aug-07	0589	Protocol Amendment: New Investigator		SP615	New and revised investigators		
20-Aug-07	0589	Protocol Amendment: New Investigator		SP902	New investigators		
20-Aug-07	0589	Protocol Amendment: New Investigator		SP904	New investigators		
21-Aug-07	0590	Initial Safety Report		SP774		2006-00066	124406
21-Aug-07	0591	Follow-up Safety Report		SP746		2007-00199	124902
21-Aug-07	0591	Follow-up Safety Report		SP746		2007-00231	118301
23-Aug-07	0592	Information Amendment: Clinical		SP903	Single-site, randomized, double-blind, placebo- and active comparator controlled single-dose crossover trial to evaluate the abuse potential of lacosamide in healthy subjects with a history of recreationally CNS depressant use		
27-Aug-07	0593	Follow-up Safety Report		SP746		2007-00244	102717
27-Aug-07	0593	Follow-up Safety Report		SP746		2007-00199	124902
27-Aug-07	0593	Follow-up Safety Report		SP830		2007-00248	114211
28-Aug-07	0594	7-Day Safety Report		SP745		2007-00255	108222
04-Sep-07	0595	Follow-up Safety Report		SP746		2007-00203	101208

Monday, November 10, 2008

IND 57,939

Page 129 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
07-Sep-07	0596		7-Day Safety Report	SP745		2007-00265	102202
07-Sep-07	0597		Follow-up Safety Report	SP830		2005-00618	105019
07-Sep-07	0597		Follow-up Safety Report	SP830		2007-00248	114211
12-Sep-07	0598		Follow-up Safety Report	SP830		2007-00248	114211
12-Sep-07	0598		Follow-up Safety Report	SP615		2005-00465	10477
12-Sep-07	0598		Follow-up Safety Report	SP746		2007-00214	105622
20-Sep-07	0599		Protocol Amendment: New Investigator	SP902	New and revised investigators		
20-Sep-07	0599		Protocol Amendment: New Investigator	SP615	Revised investigators		
20-Sep-07	0599		Protocol Amendment: New Investigator	SP904	New and revised investigators		
04-Oct-07	0600		Initial Safety Report	SP746		2007-00281	101707
15-Oct-07	0601		7-Day Safety Report	SP615		2007-00289	10180
16-Oct-07	0602		Initial Safety Report	SP756		2007-00295	15405
19-Oct-07	0603		Initial Safety Report	SP745		2007-00288	114721
19-Oct-07	0604		Information Amendment: Clinical		Investigator's Brochure dated 31-AUG-2007		

Monday, November 10, 2008

IND 57,939

Page 130 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
19-Oct-07	0605		Protocol Amendment: Change in Protocol	SP904	Amendment 1		
19-Oct-07	0605		Protocol Amendment: Change in Protocol	SP902	Amendment 1		
22-Oct-07	0606		Protocol Amendment: New Investigator	SP756	Revised Investigator		
22-Oct-07	0606		Protocol Amendment: New Investigator	SP904	New and revised investigators		
22-Oct-07	0606		Protocol Amendment: New Investigator	SP902	New and revised investigators		
25-Oct-07	0607		Initial Safety Report	SP615		2007-00292	11429
30-Oct-07	0608		Follow-up Safety Report	SP756		2007-00295	15405
01-Nov-07	0609		7-Day Safety Report	SP746		2007-00308	105621
01-Nov-07	0610		Initial Safety Report	SP774		2006-00439	100804
12-Nov-07	0611		Initial Safety Report	10053		2007-00316	SP615
14-Nov-07			General Correspondence	SP756	Email Mr. Tavarespagan, FDA, requested copy of protocol SP756		
14-Nov-07	0612		Initial Safety Report			2007-00317	101904
15-Nov-07	0613		General Correspondence		Appointment of UCB as agent in safety reporting to the IND		

Monday, November 10, 2008

IND 57,939

Page 131 of 138

<i>Submission Serial</i>		<i>Submission</i>		<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS</i>	
<i>Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Type</i>			<i>Mfr Control No</i>	<i>CIOMS Subject No</i>
21-Nov-07	0615		Protocol Amendment: New Investigator	SP902	New and revised investigators		
21-Nov-07	0615		Protocol Amendment: New Investigator	SP904	New and revised investigators		
21-Nov-07	0615		Protocol Amendment: New Investigator	SP756	New and revised investigators		
04-Dec-07	0617		Follow-up Safety Report			2007-00316	10053
04-Dec-07	0618		Follow-up Safety Report			2007-00288	114721
05-Dec-07	0619		Protocol Amendment: New Protocol	SP926	Original Protocol		
07-Dec-07	0620		General Correspondence		Notify IND that samples of dosing cups have been sent to DMETS		
20-Dec-07			General Correspondence		Email Ms. Ware, FDA, 20-DEC-07 submission, serial no. 0625		
20-Dec-07	0624		Protocol Amendment: New Investigator	SP902	New investigators		
20-Dec-07	0624		Protocol Amendment: New Investigator	SP904	New investigators		
20-Dec-07	0625		General Correspondence	LPT 20615	Request FDA concurrence on proposed dosing increase		

Monday, November 10, 2008

IND 57,939

Page 132 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
21-Dec-07			FDA Correspondence		Ms. Ware, FDA, emails nonclinical team concurs with proposal to escalate dose in juvenile dog study as described in serial no. 0625		
18-Jan-08	0628		Protocol Amendment: New Investigator	SP902	New and revised investigators		
18-Jan-08	0628		Protocol Amendment: New Investigator	SP615	Revised investigators		
18-Jan-08	0628		Protocol Amendment: New Investigator	SP756	Revised investigators		
18-Jan-08	0628		Protocol Amendment: New Investigator	SP904	New and revised investigators		
11-Feb-08	0633		General Correspondence	SP615, SP756	Report of potential misconduct under PI Dr. Robert Leroy		
22-Feb-08	0636		Protocol Amendment: New Investigator	SP904	New and revised investigators		
22-Feb-08	0636		Protocol Amendment: New Investigator	SP615	Revised investigators		
22-Feb-08	0636		Protocol Amendment: New Investigator	SP756	Revised investigator		
22-Feb-08	0636		Protocol Amendment: New Investigator	SP902	New and revised investigators		
22-Feb-08	0636		Transfer of Obligations	SP756			

Monday, November 10, 2008

IND 57,939

Page 133 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
28-Feb-08			General Correspondence		Email Ms. Ware, FDA, proposed language for updating Informed Consent based on the FDA Alert for suicidality and antiepileptic drugs		
20-Mar-08	0638		Protocol Amendment: New Investigator	SP756	New and revised investigators		
20-Mar-08	0638		Protocol Amendment: New Investigator	SP902	New and revised investigators		
20-Mar-08	0638		Protocol Amendment: New Investigator	SP904	New and revised investigators		
20-Mar-08	0638		Protocol Amendment: New Investigator	SP926	New investigator		
20-Mar-08	0638		Protocol Amendment: New Investigator	SP615	New and revised investigators		
25-Mar-08	0639		Information Amendment: CMC Data				
28-Mar-08	0640		Protocol Amendment: Change in Protocol	SP615	Amendment 9		
28-Mar-08	0640		Protocol Amendment: Change in Protocol	SP756	Amendment 3		
01-Apr-08			FDA Correspondence		Ware emails Division's response to proposed Informed Consent language		
01-Apr-08			General Correspondence		Email Ware that revised Informed Consent language will be distributed to all lacosamide INDs		

Monday, November 10, 2008

IND 57,939

Page 134 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
18-Apr-08	0642		Protocol Amendment: New Investigator	SP615	Revised investigators		
18-Apr-08	0642		Protocol Amendment: New Investigator	SP902	New and revised investigators		
18-Apr-08	0642		Protocol Amendment: New Investigator	SP904	New and revised investigators		
18-Apr-08	0642		Protocol Amendment: New Investigator	SP926	New investigator		
20-May-08	0644		Protocol Amendment: New Investigator	SP926	New and revised investigators		
20-May-08	0644		Protocol Amendment: New Investigator	SP904	New and revised investigators		
20-May-08	0644		Protocol Amendment: New Investigator	SP902	Revised investigators		
20-May-08	0644		Protocol Amendment: New Investigator	SP756	New investigator		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	MD-11-011-0012	Evaluation of potential effect of Lacosamide in the acute experimental allergic encephalomyelitis rat model		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	F-9938	Effect of lacosamide on slow inactivation in Nav 1.2 (expressed in CHO cells) Nav 1.4 and Nav 1.4 and Nav 1.4/IFM>QQQ (expressed in Xenopus oocytes)		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	847 Amend 1	Structure proposal for polar metabolite		

Monday, November 10, 2008

IND 57,939

Page 135 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	F-9945	Differential block of sensory neuronal voltage-gated sodium channels by lacosamide, lidocaine and carbamazepine. (Previously: Effect of lacosamide on recombinant Nav 1.3 and Nav 1.7 voltage-gated sodium current properties)		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	9496	Oxford Cardiac Pharmacology Ltd: Effect of lacosamide on action potential parameters (including Vmax, the maximal rate of rise) in guinea pig ventricular myocytes		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	0699/069	(14C)-SPM 927: A study of absorption and excretion following single oral administration to the rabbit		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	LPT 20614/06	6-Week Dose-Range-Finding Study for a 33-Week Chronic Toxicity Study of SPM 927 by Repeated Oral Administration to Juvenile Beagle Dogs		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	F-9928	Determination of interaction of lacosamide with the antiepileptic drugs carbamazepine, Phenytoin, sodium valproate, lamotrigine, levetiracetam, topiramate and gabapentin		
28-May-08	0646		Information Amendment: Pharmacology/Toxicology	SCHW 004	Evaluation of Lacosamide in an animal model for obsessive compulsive disorder: marble burying		
20-Jun-08	0648		Protocol Amendment: New Investigator	SP615	Revised investigators		

Monday, November 10, 2008

IND 57,939

Page 136 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Jun-08	0648		Protocol Amendment: New Investigator	SP902	New and revised investigators		
20-Jun-08	0648		Protocol Amendment: New Investigator	SP756	New investigator		
20-Jun-08	0648		Protocol Amendment: New Investigator	SP904	New and revised investigators		
24-Jun-08	0649		Annual Report		Period covering March 26, 2007 through March 25, 2008		
22-Jul-08	0650		Protocol Amendment: New Investigator	SP756	New and revised investigators		
22-Jul-08	0650		Protocol Amendment: New Investigator	SP902	New and revised investigators		
22-Jul-08	0650		Protocol Amendment: New Investigator	SP904	Revised investigators		
22-Jul-08	0650		Protocol Amendment: New Investigator	SP615	New and revised investigators		
20-Aug-08	0651		Protocol Amendment: New Investigator	SP904	New and revised investigators		
20-Aug-08	0651		Protocol Amendment: New Investigator	SP902	New and revised investigators		
20-Aug-08	0651		Protocol Amendment: New Investigator	SP615	Revised investigator		
20-Aug-08	0651		Protocol Amendment: New Investigator	SP926	New investigators		

Monday, November 10, 2008

IND 57,939

Page 137 of 138

<i>Submission Date</i>	<i>Serial No</i>	<i>Location</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title/ Description</i>	<i>CIOMS Mfr Control No</i>	<i>CIOMS Subject No</i>
20-Aug-08	0651		Protocol Amendment: New Investigator	SP756	Revised investigators		
22-Sep-08	0655		Protocol Amendment: New Investigator	SP902	Revised investigators		
22-Sep-08	0655		Protocol Amendment: New Investigator	SP756	Revised investigators		
22-Sep-08	0655		Protocol Amendment: New Investigator	SP904	New and revised investigators		
07-Oct-08	0657		Protocol Amendment: Change in Protocol	SP902	Amendment 2		
07-Oct-08	0657		Protocol Amendment: Change in Protocol	SP904	Amendment 2		
08-Oct-08	0659		General Correspondence	SP902, SP904	Request IRB Waiver for SP902 and SP904		
09-Oct-08	0660		Protocol Amendment: Change in Protocol	SP926	Amendment 1		

NDA 22-253 Submissions

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
28-Sep-07		General Correspondence		Email Ms. Ventura, FDA, to notify of problem with disk 3 of original NDA submission
28-Sep-07	0000	Original NDA		
01-Oct-07		FDA Correspondence		Ms. Ventura, FDA, emails to send replacement disks
01-Oct-07		General Correspondence		Email Ms. Ventura, FDA, that replacement disks will be sent
01-Oct-07		Other		Replace disks 1 of 9 and 3 of 9 in original NDA submission
01-Oct-07		FDA Correspondence		Ms. Ventura, FDA, emails to mention her in cover letter with replacement disks
22-Oct-07		FDA Correspondence		FDA mails letter acknowledging NDA 22-253 for epilepsy and NDA 22-284 for neuropathic pain
20-Nov-07		FDA Correspondence		Ms. Ware, FDA, emails request from clinical pharmacology group related to initial filing review of the lacosamide applications
26-Nov-07	0001	Response to FDA Request for Information		Submit response to 20-NOV-2007 clinical pharmacology request
10-Dec-07		FDA Correspondence		Dr. Katz, FDA, sends letter accepting NDA for filing
13-Dec-07		Amendment to a Pending Application		Submit additional clinical pharmacology responses
13-Dec-07	0002	Amendment to a Pending Application		Response to request: clinical pharmacology; provide responses not included in 0001
19-Dec-07		General Correspondence		Email Ms. Ware, FDA, preliminary responses to 74-day letter
07-Jan-08		FDA Correspondence		Ms. Ware, FDA, emails request from clinical and statistical team for additional datasets
07-Jan-08		General Correspondence		Email Ms. Ware, FDA, that requested datasets were sent on DVD via courier
14-Jan-08		FDA Correspondence		Ms. Ware, FDA, emails requests from DNP's clinical team related to ongoing review of lacosamide applications

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
15-Jan-08		General Correspondence		Email Ms. Ware, FDA, for additional explanation on clinical questions received 14-JAN-2008
15-Jan-08		FDA Correspondence		Ms. Ware, FDA, emails responses from email information request related to 14-JAN-2008 FDA email
16-Jan-08		General Correspondence		Email Ms. Ware, FDA, summary of 16-JAN-2008 conversation discussing GCP inspections
16-Jan-08		FDA Correspondence		Mr. Sullivan, FDA, emails outstanding clinical pharmacology items
17-Jan-08		FDA Correspondence		Ms. Gunther, FDA, emails information request for potential inspection sites
23-Jan-08	0003	Amendment to a Pending Application		120-day safety update and 74-day letter responses
29-Jan-08		FDA Correspondence		Ware emails request form DNP's clinical team for a summary table of AE that led to dose reduction and/or discontinuation by SOC and PT in Pool EP S1 by dose at onset
31-Jan-08		FDA Correspondence		Ms. Ware, FDA, emails request from DNP's clinical team
06-Feb-08		FDA Correspondence	SP742, SP743, SP768	Sullivan emails request additional analyses for SP742, SP743, and SP768
07-Feb-08		FDA Correspondence		Sheryl Gunther, FDA, emails request for addresses for investigators Nischik, Pojakovic, and Hajnsek
08-Feb-08		Response to FDA Request for Information		Send Ms. Gunther, FDA, background investigator information requested 17-JAN-2008
08-Feb-08		General Correspondence		Email Ms. Gunther, FDA, contact information requested 07-FEB-2008
08-Feb-08		FDA Correspondence		Ms. Gunther, FDA, emails thanks for contact information
08-Feb-08		General Correspondence		Email Ms. Ware, FDA, partial responses to questions received 14-JAN-2008 and 31-JAN-2008
12-Feb-08		General Correspondence		Email Ms. Ware, FDA, additional partial responses to questions received 14-JAN-2008 and 31-JAN-2008
13-Feb-08	0004	Amendment to a Pending Application		Response to request: clinical; respond to questions received 15-JAN, 29-JAN, and 31-JAN-2008

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
14-Feb-08		General Correspondence		Email Ms. Ware, FDA, that one request from 14-FEB-2008 email is addressed in lifecycle received today and the other will be reviewed
14-Feb-08		FDA Correspondence		Ms. Ware, FDA, emails requests from DNP's clinical team
22-Feb-08		General Correspondence		Email Ms. Ware, FDA, responses to request from 14-FEB-2008 email
25-Feb-08	0005	Amendment to a Pending Application		Response to request: clinical; respond to 31-JAN-2008, 06-FEB-2008, and 14-FEB-2008 email requests
26-Feb-08		FDA Correspondence		Ms. Ware emails request from DNP's clinical pharmacology team
03-Mar-08		FDA Correspondence		Ms. Ware, FDA, emails requests from DNP's clinical team
05-Mar-08		FDA Correspondence		Email Ms. Ware, FDA, response to one of the request received 03-MAR-2008
05-Mar-08		General Correspondence		Email Ms. Ware, FDA, response to request received 26-FEB-2008
06-Mar-08		FDA Correspondence		Sullivan emails request from DAARP team for narratives for all patients with AEs of syncope of presyncope and tables comparing frequency of event by treatment group
07-Mar-08		FDA Phone Contact		Discuss NDA reviews with Ms. Ware, FDA
07-Mar-08		FDA Correspondence	SP754	Ware emails requests from DNP's clinical team; request additional detail on subject 75411401 and clarification of footnote in cardiac report
10-Mar-08		General Correspondence		Email Ms. Ware, FDA, clarification on 03-MAR-2008 request
10-Mar-08		Response to FDA Request for Information		Submit requested ECG data for subjects in EP Pool S1
11-Mar-08		General Correspondence		Request Ms. Ware forward 11-MAR-2008 email to Dr. Vallalba
11-Mar-08		FDA Correspondence		Mr. Sullivan emails on behalf of Ms. Ware request for additional analyses
11-Mar-08		General Correspondence		Email Dr. Vallalba and Ms. Ware password for response to request for EP pool S1 dataset from ISS
13-Mar-08		FDA Correspondence	SP903	Sullivan emails request from the stats reviewer for clarification on abuse liability study's dataset
20-Mar-08		FDA Correspondence		Dr. Sood, FDA, mails information request letter regarding drug substance and drug product

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
20-Mar-08	0006	Amendment to a Pending Application		Response to Request: Clinical; respond to 04-MAR-2008 teleconference request and 13-MAR-2008 email; also respond to email requests 26-FEB-2008, 03-MAR-2008, 07-MAR-2008, 11-MAR-2008; provide draft blister labels and cartons requested in 74-day letter
20-Mar-08		FDA Correspondence		Sullivan emails CMC IR letter that applies to drug substance, tablet, and IV drug product
31-Mar-08		FDA Correspondence		Sullivan emails request to resubmit ISS lab1.xpt and lab2.xpt datasets as separate files
02-Apr-08		FDA Correspondence		Ware emails requests from DNP's statistical team
03-Apr-08	0007	Amendment to a Pending Application		Response to Request: Clinical; respond to 07-MAR-2008 email request for clarification on subject 75411401 and 31-MAR-2008 email request for lab datasets
03-Apr-08		FDA Correspondence		Ware emails requests from DNP's statistical team
04-Apr-08		General Correspondence		Email Ware if there is any update regarding CSS and the tradename and notify that revised label/container cartons will be sent next week
04-Apr-08		FDA Correspondence		Ware emails that labeling submission next week is acceptable; would like to speak about updates from internal meeting
04-Apr-08		FDA Correspondence		Ware adds additional comment to email sent earlier today
04-Apr-08		General Correspondence		Email Ware receipt of 04-APR-2008 comments regarding impurity specifications
04-Apr-08		FDA Correspondence		Ware emails comments from ONDQA and OND non-clinical review teams related to proposed impurity specifications
04-Apr-08		General Correspondence		Email Ware agreement to be available 07-APR-2008 between 1pm and 3pm to discuss internal FDA meeting
07-Apr-08		General Correspondence		Email Ware clarification on symbol in 04-APR-2008 request
07-Apr-08		FDA Correspondence		Ware emails agreement to clarification on symbol in 04-APR-2008 request
09-Apr-08	0008	Amendment to a Pending Application		Revised labeling - excluding package insert
11-Apr-08		General Correspondence		Email Ware responses to questions emailed 04-APR-2008 on drug substance and IV/syrup formulation

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
11-Apr-08		General Correspondence		Email Ware responses to 02-APR-2008 statistical questions
14-Apr-08	0009	Amendment to a Pending Application		Response to Request: Clinical; respond to 06-MAR-2008 and 07-MAR-2008 clinical email requests for narratives for all neuropathic pain subjects with syncope or presyncope; provide narratives for migraine study dropouts as requested in 11-MAR-2007 email
16-Apr-08		FDA Correspondence		Ware emails request from DNP's clinical team regarding overall exposure to lacosamide and placebo in all studies
18-Apr-08		FDA Correspondence	SP755, SP774, SP757	Ware emails request from DNP's clinical team regarding patients 170106 and 17011
18-Apr-08		Amendment to a Pending Application		Provide responses to requests in CMC letter dated 20-MAR-2008 and emails dated 02-APR-2008 and 04-APR-2008
18-Apr-08	0010	Amendment to a Pending Application		Respond to 20-MAR-2008 CMC request and 02-APR-2008 and 04-APR-2008 email requests
25-Apr-08		FDA Correspondence		Ware emails request from DNP's CMC review team
25-Apr-08		FDA Correspondence		Ware emails request from DNP's clinical team regarding subject 588/8061
28-Apr-08		General Correspondence		Email Ware Schwarz commitments following 23-APRIL-2008 teleconference regarding oral syrup dosing
29-Apr-08		FDA Correspondence		Sullivan emails request for narratives of patients with AE dyskinesia
30-Apr-08	0011	Amendment to a Pending Application		Respond to requests received 20-MAR-2008, 16-APR-2008, and 18-APR-2008
30-Apr-08		Response to FDA Request for Information	1106	Email Ware partial response to 25-APRIL-2008 email request regarding CMC data
06-May-08		FDA Correspondence		Sullivan emails request from reviewer of Environmental Assessment to submit a non-confidential EA
07-May-08		FDA Correspondence		Ware emails request from DNP's clinical team requesting narratives and CRFs for four patients who discontinued due to cardiac or ECG issues; ECGs for 755122303; suicidality information on 754/12512
08-May-08		Response to FDA Request for Information		Email Ware dyskinesia narratives requested in 29-APRIL-2008 email

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
09-May-08	0012	Amendment to a Pending Application		Response to requests; respond to nonclinical question in 25-APR-2008 email and provide revision to environmental assessment requested in 06-MAY-2008 email
12-May-08		General Correspondence		Email Ware that 12-MAY-2008 requests have been received
12-May-08		FDA Correspondence		Ware emails requests from DNP's clinical team
12-May-08		FDA Correspondence		Ware emails request from chemistry review team regarding NDA 22-254 and NDA 22-255
13-May-08		Response to FDA Request for Information		Email Ware AE report responding to 25-APRIL-2008 email request regarding subject 588-8061
13-May-08		General Correspondence		Email Ware requested laboratory results for subject 588/5061
16-May-08		Response to FDA Request for Information		Email Ware response to questions 2, 3, and 4 from 12-MAY-2008 email request
16-May-08		Response to FDA Request for Information		Email Ware responses to bullets 1 and 2 from 07-MAY-2008 email request regarding narratives and CRFs and ECG data
16-May-08		General Correspondence		Email Ware question/proposal regarding request number 5 from 12-MAY-2008 email request
16-May-08		FDA Correspondence		Ware emails request from clinical reviewer for clarification on tables EP 5.1.1 and EP 5.1.2 from partial response to 12-MAY-2008 request
19-May-08		Response to FDA Request for Information		Email Ware response to bullet 3 from 07-MAY-2008 email request regarding subject 754/12512 suicidality
19-May-08		Response to FDA Request for Information		Email Ware partial response to 16-MAY-2008 email request and suggest teleconference if response is not sufficient
20-May-08		FDA Correspondence	SP643	Ware emails requests from clinical pharmacology review team regarding SP643 and analytical assay validation methods
20-May-08		FDA Phone Contact		TC with Gary Gensinger and Jackie Ware to discuss eCTD issues
21-May-08		FDA Correspondence		Ware emails WORD document of example table for requested summary information on analytical assay validation methods
22-May-08		FDA Correspondence		Ware emails request from clinical review team for additional information on subject 588/8061

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
23-May-08		General Correspondence		Email Ware response to 22-MAY-2008 request for information on subject 588/5061
23-May-08		Response to FDA Request for Information		Email Ware response to email request received 22-MAY-2008 regarding subject 588/8061
27-May-08		Response to FDA Request for Information	SP643	Email Ware responses to clinical pharmacology requests received in 20-MAY-2008 email regarding subject classification in SP643 and analytical assay validation methods
27-May-08	0013	Amendment to a Pending Application		Response to requests in 25-APR-2008, 29-APR-2008, 07-MAY-2008, 12-MAY-2008, 16-MAY-2008, and 22-MAY-2008 emails
30-May-08		FDA Phone Contact		Ware calls to request WORD copy of draft labeling; also discuss review items: scheduling, labels, post-marketing requests, REMS, pediatrics, class labeling
02-Jun-08		FDA Correspondence		Ware emails question about 02-JUNE-2008 response to 12-MAY-2008 question 1
04-Jun-08		General Correspondence		Email Ware concomitant disease tables requested 12-MAY-2008
06-Jun-08		FDA Correspondence		Ware emails request for teleconference 12-JUNE-2008 at 10:15 to discuss potential cases of multi-organ hypersensitivity
11-Jun-08		FDA Correspondence	SP830	Ware emails request for additional information on subject SP830/11201 and request for database search for all cases of potential multiorgan hypersensitivity reactions
11-Jun-08	0014	Amendment to a Pending Application		Respond to requests received 12-MAY-2008 and 2-JUN-2008
26-Jun-08		FDA Phone Contact		Ware calls to discuss review with goal of reaching an actio by 29-JUL-2008, dependent on review of multi-organ hypersensitivity data; also discuss labeling
30-Jun-08		Meeting Request		Type A meeting request to discuss abuse potential of lacosamide
02-Jul-08		FDA Correspondence		Ware emails comments from controlled substance staff with conclusion that lacosamide has abuse potential similar to alprazolam, a schedule IV drug
03-Jul-08		General Correspondence		Email Ware requested documents
10-Jul-08		General Correspondence		Email Sullivan to ask when to expect draft labeling from DAARP
10-Jul-08		General Correspondence		Email Ware response to multiorgan hypersensitivity issue raised in 06-JUN-2008 email, 11-JUN-2008 email, and 12-JUN-2008 teleconference

<i>Submission Date</i>	<i>Sequence No</i>	<i>Submission Type</i>	<i>Study No</i>	<i>Title of Report</i>
11-Jul-08		General Correspondence		Email Ware pediatric development document
11-Jul-08	0015	Amendment to a Pending Application		Response to requests; respond to request in 11-JUN-2008 teleconference to search for cases of multi-organ hypersensitivity based on defined criteria; final part of response to 12-MAY-2008 CMC request; and Type A meeting request
12-Jul-08		General Correspondence		Email Leah Ripper, FDA, table showing financial disclosure cutoff dates by trial.
12-Jul-08		Response to FDA Request for Information		Email Ms. Ripper, FDA, table of enrollment and last subject dates in response to financial disclosure request
14-Jul-08		FDA Correspondence		Ripper emails that financial disclosure information emailed 12-JUL-2008 addresses her concern
15-Jul-08		General Correspondence		Ware emails that DAARP and DNP labeling comments will be combined
15-Jul-08		FDA Correspondence		Ware emails that DNP and DAARP labeling comments will likely be combined
17-Jul-08	0016	Amendment to a Pending Application		Response to requests; provide case report forms related to 0015 submission
18-Jul-08		FDA Phone Contact		Teleconference to discuss multi-organ hypersensitivity and three month extension of review clock
21-Jul-08		General Correspondence		Email Ware request for copy of full Eight Factor Analysis prepared by CSS
21-Jul-08		General Correspondence		Email Ms. Ware request for copy of Eight Factor Analysis prepared by CSS to determine lacosamide's scheduling
22-Jul-08		General Correspondence		Email Ware requesting discussion on CSS analysis, potential extension of PDUFA date, clinical hold, and safety update
25-Jul-08		FDA Correspondence		Ware emails list of additional search terms suggestive or internal organ involvement
25-Jul-08		FDA Phone Contact		SB calls Ware to discuss additional terms for multiorgan hypersensitivity, extension of action date, CSS analysis, safety update, pediatric clinical hold, and draft label
25-Jul-08		General Correspondence		Email Sullivan to ask if Action letter for LCM for pain will be a Complete Response letter or the old style of approvable or not approvable
25-Jul-08		FDA Correspondence		Ware emails the Action letter for pain indication should be issued based on the old regulations

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28-Jul-08		General Correspondence		Email Ware request from medical colleagues for clarity on inclusion of preferred terms hepatitis and hypersensitivity in multiorgan hypersensitivity analysis
28-Jul-08		FDA Correspondence		Sare Stradley emails "Not Approvable" letter for 22-284
29-Jul-08		General Correspondence		Email Ware and Sullivan lifecycle 0017, response to 22-284 action letter received 28-JUL-2008, meeting request, and request for extension of review period
29-Jul-08		FDA Correspondence		Stradley emails that FDA will be in touch about scheduling meeting requested 29-JUL-2008
30-Jul-08	0017	Amendment to a Pending Application		Request for extension of review period; meeting request
30-Jul-08		General Correspondence		Email Ware supporting data for subject 588/8061 where the bilirubin value was normal
31-Jul-08		FDA Correspondence		Ware emails request for laboratory value criteria clarification
31-Jul-08		FDA Correspondence		Nighswander mails PDUFA extension letter for epilepsy indications
01-Aug-08	0018	Amendment to a Pending Application		Response to requests; provide proposed questions for Type A meeting requested 30-JUN-2008; provide location of CRF data for subject 588/8061; submit high level pediatric development plan
01-Aug-08		FDA Correspondence		Ware emails request from DNP's clinical team to clarify the denominators used in the search for potential multi-organ hypersensitivity
04-Aug-08		FDA Phone Contact		Stradley calls to discuss meeting on Not Approvable letter for the pain indication
06-Aug-08		FDA Correspondence		Sullivan emails that 22-284 meeting request is considered a Type A meeting but usually can't be granted in requested time frame
06-Aug-08		FDA Correspondence		Ware emails comments from Controlled Substance Staff in response to 31-JUL-2008 request
07-Aug-08		General Correspondence		Email Ware clarification question on CSS analysis
11-Aug-08		General Correspondence		Email Ware requested normal lab values for subject 588/8061

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14-Aug-08	0019	Amendment to a Pending Application		Response to requests; respond to 18-JUL2008 teleconference and 25-JUL and 31-JUL email requests for addition of search terms and criteria to multi-organ hypersensitivity search; provide normal lab values for subject 588/8061 as requested 31-JUL-2008
19-Aug-08		General Correspondence		Email Ware questions regarding meeting package to be sent for 29-SEP-2008 meeting
19-Aug-08		General Correspondence		Email Ware request for cardiac section of the draft label and question on pediatric drug development
21-Aug-08		General Correspondence		Email Ware response to 01-AUG-2008 request for multi-organ hypersensitivity information
21-Aug-08		FDA Phone Contact		Discussion of meeting with DNP/CSS on scheduling and to discuss responses to questions previously asked
27-Aug-08	0020	Amendment to a Pending Application		Response to requests; respond to 01-AUG-2008 email request for clarification on multi-organ hypersensitivity reaction denominators; provide revised blister labels
04-Sep-08	0021	Meeting Package		Information package for Type A meeting on September 29, 2008
10-Sep-08		General Correspondence		Email Ware that response to multi-organ hypersensitivity request was sent as life cycle 19 on 14-AUG-2008
23-Sep-08	0022	Amendment to a Pending Application		Meeting Package for Type A meeting on October 16, 2008
26-Sep-08		General Correspondence		Email Sullivan letter from Schwarz to EMEA withdrawing the lacosamide pain application
26-Sep-08		FDA Correspondence		Ware emails Agency's preliminary responses to questions for 29-SEP-2008 meeting
29-Sep-08		FDA Correspondence		Sullivan emails that 15 desk copies will be required for 16-OCT-2008 meeting package
30-Sep-08		General Correspondence		Email Sullivan that meeting package for 16-OCT-2008 meeting will be sent via email today and as a lifecycle tomorrow, 01-OCT-2008
01-Oct-08		FDA Correspondence		Sullivan emails thanks for PDF of 16-OCT-2008 meeting package and provides mailing address for desk copies
03-Oct-08		FDA Correspondence		Ware emails list of FDA attendees from 29-SEP-2008 meeting

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08-Oct-08		General Correspondence		Email Ware meeting minutes and meeting slides from 29-SEP-2008 meeting with DNP and CSS
10-Oct-08		General Correspondence		Email Ware letter from Patty Fritz requesting teleconference to discuss scheduling
14-Oct-08		FDA Correspondence		Dr. Throckmorton emails to notify that Agency is discussing how best to handle teleconference requested 10-OCT-2008
15-Oct-08	0023	Amendment to a Pending Application		Reply to FDA preliminary response to questions submitted in life cycle 0021 concerning CSS recommendations of C-IV scheduling
17-Oct-08		General Correspondence		Email Ware proposed REMS form
21-Oct-08		FDA Phone Contact		Ware returned call to discuss issues from label review, including storage conditions, safety pharmacology section, CSS class, suicidality, and post-marketing commitments
21-Oct-08	0024	Amendment to a Pending Application		Proposed REMS
23-Oct-08		General Correspondence		Email Ware response to Division label changes and proposals for consideration as well as a justification document for the sponsor-requested changes
23-Oct-08		FDA Correspondence		Ware emails post-marketing commitments and labeling revisions
27-Oct-08		General Correspondence		Email Ware analysis requested at 27-OCT-2008 meeting for PR outliers
29-Oct-08		FDA Correspondence		Ware emails complete response letter for 22-255 and approval letter for 22-253 and 22-254
30-Oct-08	0025	Amendment to a Pending Application	SP903	Response to request; additional information requested in 20-OCT-2008 teleconference by Dr. Throckmorton from SP903, abuse liability trial